Journal of
THE CHEMICAL SOCIETY

Committee of Publication :

Chairman : Sir Cyril Hinshelwood, M.A., Sc.D., D.Sc., F.R.S.

Sir Wallace Akers, C.B.E., B.A., D.Sc., F.R.I.C.
C. E. H. Bawn, B.Sc., Ph.D.
D. J. Bell, Sc.D., Ph.D., F.R.I.C.
R. P. Bell, M.A., B.Sc., F.R.S.
F. Bergel, D.Phil.Nat., D.Sc., F.R.I.C.
E. J. Bowen, M.A., D.Sc., F.R.S.
H. Burton, Ph.D., D.Sc., F.R.I.C.
A. H. Cook, D.Sc., F.R.I.C., F.R.S.
C. A. Coulson, M.A., D.Sc., F.R.S.
F. S. Dainton, M.A., Ph.D.
C. W. Davies, D.Sc., F.R.I.C.
M. G. Evans, D.Sc., F.R.S.
F. Fairbrother, D.Sc.
D. Ll. Hammick, M.A., D.Sc.
R. D. Haworth, D.Sc., Ph.D., F.R.S.
E. D. Hughes, D.Sc., F.R.I.C., F.R.S.
R. P. Linstead, C.B.E., M.A., D.Sc., F.R.S.
F. G. Mann, Sc.D., F.R.I.C., F.R.S.
H. W. Melville, Ph.D., D.Sc., F.R.S.
L. N. Owen, Ph.D., D.Sc., F.R.I.C.
S. Peat, Ph.D., D.Sc., F.R.S.
Sir Eric Rideal, M.B.E., M.A., D.Sc., F.R.S
J. M. Robertson, M.A., D.Sc., F.R.S.
H. N. Rydon, D.Sc., D.Phil., F.R.I.C.
C. W. Shoppee, D.Sc., D.Phil., F.R.I.C.
R. Spence, Ph.D., D.Sc., F.R.I.C.
L. E. Sutton, M.A., D.Phil., F.R.S.
A. R. Todd, M.A., D.Sc., F.R.S.
J. Walker, Ph.D., D.Phil., D.Sc.
W. Wardlaw, C.B.E., D.Sc., F.R.I.C.
W. A. Waters, M.A., Sc.D., F.R.I.C.
T. S. Wheeler, Ph.D., D.Sc., F.R.I.C.
F. G. Young, M.A., D.Sc., F.R.S.

Editor :

R. S. Cahn, M.A., D.Phil.Nat., F.R.I.C.

Assistant Editors :

A. D. Mitchell, D.Sc., F.R.I.C.
L. C. Cross, Ph.D., A.R.C.S., F.R.I.C.

Indexer :

Margaret Le Pla, B.Sc.

AUGUST, 1951

Subscription rate to non-Fellows £6 0s. 0d. per annum post free.

LONDON: THE CHEMICAL SOCIETY, BURLINGTON HOUSE, W.1

THE CHEMICAL SOCIETY

PATRON:

HIS MAJESTY THE KING

President:

SIR ERIC RIDEAL, M.B.E., M.A., D.Sc., F.R.S.

Vice-Presidents

who have filled the office of President:

F. G. DONNAN, C.B.E., D.Sc., LL.D., F.R.S.
SIR IAN HEILBRON, D.S.O., D.Sc., LL.D., F.R.S.
SIR CYRIL HINSHELWOOD, M.A., Sc.D., F.R.S.
W. H. MILLS, M.A., Sc.D., F.R.S.
SIR ROBERT ROBINSON, O.M., D.Sc., LL.D., F.R.S.
N. V. SIDGWICK, C.B.E., D.Sc., LL.D., F.R.S.

Vice-Presidents:

G. R. CLEMO, D.Phil., D.Sc., F.R.S.
J. W. COOK, D.Sc., F.R.I.C., F.R.S.
D. H. HEY, Ph.D., D.Sc., F.R.I.C.
R. P. LINSTEAD, C.B.E., M.A., D.Sc., F.R.S.
M. STACEY, Ph.D., D.Sc., F.R.S.
W. WARDLAW, C.B.E., D.Sc., F.R.I.C.

Treasurer:

SIR WALLACE AKERS, C.B.E., B.A., D.Sc., F.R.I.C.

Secretaries:

H. BURTON, Ph.D., D.Sc., F.R.I.C.
E. D. HUGHES, D.Sc., F.R.I.C., F.R.S.
L. E. SUTTON, M.A., D.Phil., F.R.S.

Ordinary Members of Council:

J. S. ANDERSON, M.Sc., Ph.D., A.R.C.S.
G. BADDELEY, M.Sc., Ph.D., D.Sc.
WILSON BAKER, M.A., D.Sc., F.R.S.
C. E. H. BAWN, B.Sc., Ph.D.
J. BELL, D.Sc., Ph.D., F.R.I.C.
R. P. BELL, M.A., B.Sc., F.R.S.
S. J. GREGG, Ph.D., A.R.C.S., F.R.I.C.
L. HUNTER, Ph.D., D.Sc., F.R.I.C.
F. E. KING, M.A., D.Phil., D.Sc.
L. N. OWEN, Ph.D., D.Sc., F.R.I.C.
E. G. V. PERCIVAL, Ph.D., D.Sc., F.R.I.C.
H. M. POWELL, M.A., B.Sc.
J. D. ROSE, M.A., B.Sc.
H. N. RYDON, D.Sc., D.Phil., F.R.I.C.
C. W. SHOPPEE, D.Sc., D.Phil., F.R.I.C.
J. W. SMITH, Ph.D., D.Sc., F.R.I.C.
R. SPENCE, Ph.D., D.Sc., F.R.I.C.
T. S. STEVENS, B.Sc., D.Phil., A.R.I.C.
A. R. J. P. UBBELOHDE, M.A., D.Sc., F.R.S.
A. I. VOGEL, D.Sc., D.I.C., F.R.I.C.
J. WALKER, Ph.D., D.Phil., D.Sc.
W. A. WATERS, M.A., Sc.D., F.R.I.C.

Ex-Officio Members of Council:

H. E. COX, D.Sc., Ph.D., F.R.I.C. (*Chairman of the Joint Library Committee*).
A. FINDLAY, C.B.E., D.Sc., LL.D., F.R.I.C. (*Chairman of the Chemical Council*).
L. H. LAMPITT, D.Sc., F.R.I.C. (*Chairman of the Bureau of Abstracts*).

General Secretary:
J. R. RUCK KEENE, M.B.E., T.D., B.A.

Librarian:
A. E. CUMMINS.

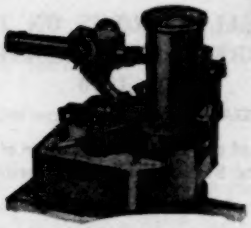
Telephone Numbers: Regent 1675/6

UNICAM INSTRUMENTS

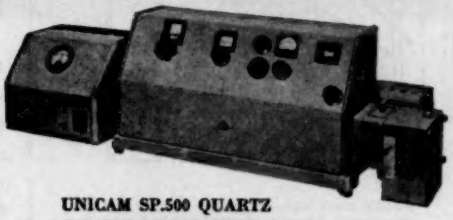
—THE TOOLS FOR THE JOB

Instruments made by Unicam fall mainly into two classes, spectrophotometers for ultraviolet, visible and infrared absorption measurements, and goniometers and powder cameras for the analysis of crystal structure. Their designs have been evolved to meet the requirements of eminent specialists and they are well adapted for a wide variety of applications in research, routine analysis and process control.

UNICAM DIFFRACTION GRATING SPECTROPHOTOMETER is a most useful instrument for clinical and chemical laboratories where its accuracy, speed and convenience in use are features of primary importance.



S.25 SINGLE CRYSTAL X-RAY GONIOMETER
This is the standard instrument for oscillation, rotation and Laue photographs. It is available with a range of accessories for a variety of techniques.



UNICAM SP.500 QUARTZ SPECTROPHOTOMETER
is a well-known instrument for the measurement of absorption between 2,000 Å and 10,000 Å. It is used in both academic and industrial laboratories the world over.

ULTRAVIOLET AND VISIBLE SPECTROPHOTOMETERS • INFRARED DETECTORS AND SPECTROMETERS • COLORIMETERS AND MICROTOMES • X-RAY AND OPTICAL GONIOMETERS FOR CRYSTAL STRUCTURE ANALYSIS • X-RAY POWDER CAMERAS INCLUDING HIGH TEMPERATURE CAMERAS

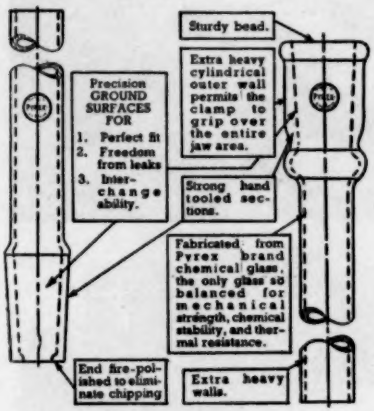
Full details will gladly be sent on request

UNICAM INSTRUMENTS (CAMBRIDGE) LTD · ARBURY WORKS · CAMBRIDGE

U164

Improved
PYREX Brand
Standard Taper
Interchangeable
Ground Glass Joints

THIS practical development of PYREX Brand Scientific Glassware, is strictly in accordance with B.S.S. No. 572/1950. It greatly increases the ease of apparatus assembly. These straight outer joints make easier and surer clamping and save time, trouble and breakages. Their extra heavy wall tubing, strong hand-tooled sections and controlled annealing mean added service life.


Sturdy bead.
Extra heavy cylindrical outer wall permits the clamp to grip over the entire jaw area.
Precision GROUND SURFACES FOR
1. Perfect fit
2. Freedom from leaks
3. Inter-change-ability.
Strong hand tooled sections.
Fabricated from Pyrex brand chemical glass, the only glass so balanced for mechanical strength, chemical stability, and thermal resistance.
End fire-polished to eliminate chipping
Extra heavy walls.

PYREX Brand Scientific Glassware is supplied only through Laboratory Furnishers, but illustrated catalogue and two free copies of our Chemist's Notebook will be sent direct on application to us.

PYREX
Regd. Trade Mark BRAND
Laboratory and Scientific Glassware

JAMES A. JOBLING & CO. LTD.,
Wear Glass Works, Sunderland.
S 3809

LITMUS
and other
TEST PAPERS
for
***p*H**
determination

•

DESCRIPTIVE LEAFLET
WILL BE SENT
FREE ON REQUEST

JOHNSONS OF HENDON LTD
335 HENDON WAY · LONDON, N.W 4
37 BROWN STREET · MANCHESTER 2
64 KINGSTON STREET · GLASGOW S

ANNUAL REPORTS ON THE PROGRESS ON CHEMISTRY FOR 1950

Volume XLVII **Published August 1st, 1951**

Copies of this regular publication of The Chemical Society may now be ordered.

Price : Twenty-five shillings, post free.

THE CHEMICAL SOCIETY
BURLINGTON HOUSE · LONDON · W.1

Telephone: **Clerkenwell 2908**

REGISTERED TRADE MARK

Telegraphic Address: **"Gasthermo, Barb, London."**

B. BLACK & SON, LTD.
180, Goswell Road, London, E.C.1.

Fluid-in-Glass Thermometers, graduated on stem, for determining temperatures between – 200°C./+ 550°C. with an accuracy, corrections and permanency well within the limits permissible to obtain N.P.L. Certificates.
The filling in the etching is least resisting and is insoluble in all solvents with the exception of those that attack the glass itself.
Makers of Calorimeter Thermometers, also Hortvet Thermometers for freezing point depressions, etc., etc.
Of all the principal Scientific Instrument and Laboratory Apparatus Manufacturers.

by the dram or by the drum

The chemist's achievement is so often the engineer's problem — for the engineer must build the plant to produce in bulk the chemical compounds which the chemist, by painstaking research, has synthesised in the test-tube. Seemingly there is no limit to the rapidly growing demands of industry for chemical raw materials; it was to meet this demand that chemists and engineers united to build the Shell chemical plant at Stanlow — a laboratory bench on a gargantuan scale. The petroleum-derived chemicals produced at Stanlow conform to the highest standards of purity and an undeviating specification. Acetone, methyl ethyl ketone, methyl isobutyl ketone, diacetone alcohol, secondary butyl alcohol and isopropyl ether among them, they are making a valuable contribution to Britain's industrial output.

SHELL **Shell Chemicals**

SHELL CHEMICALS LIMITED, Norman House, 105-109 Strand, London W.C.2.
(DISTRIBUTORS)

IN2

WHATMAN High Grade **FILTER PAPERS**

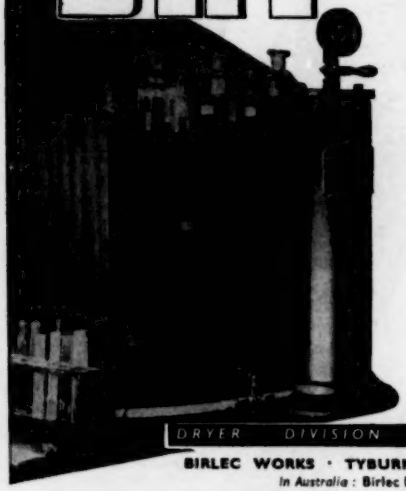
Made in England by
W. & R. BALSTON LTD.
MAIDSTONE, KENT

FOR CHROMATOGRAPHY

It has now become standard practice to use WHATMAN filter papers for this comparatively new method of analysis. We specially recommend WHATMAN grades Nos. 1, 3MM, 4, 7, 11 and 54, which have proved eminently suitable for this type of work. All these grades can be obtained in convenient size sheets from laboratory furnishers. In case of any difficulty in obtaining supplies quickly, please write to the Sole Mill Representatives :-

H. REEVE ANGEL & CO. LTD., 9 Bridewell Place, London, E.C.4

DRY gas in the laboratory



Many laboratory investigations which would be upset by moisture vapour in the air or in process gases are smoothed out by LECTRODRYERS.

- ✱ Vials, ampoules, etc. are purged with dry nitrogen.
- ✱ Delicate instruments are unaffected by variable weather.
- ✱ Catalytic gas reactions are standardised.
- ✱ Hydrogen atmosphere furnaces give consistent results.

LECTRODRYERS are economical, reliable, non-chemical moisture adsorbers which can reduce the humidity of air or other gases to any desired degree and on any scale. Special types are used for humidity control in storage and work rooms, others for drying compressed gases, and preventing the entry of moisture to acid tanks.

Let us send you detailed data relating to your problem.

BIRLEC

DRYER DIVISION of BIRLEC LIMITED

BIRLEC WORKS · TYBURN ROAD · BIRMINGHAM, 24
In Australia : Birlec Limited, Sydney, N.S.W.

BM/B.596a

BEATSON CLARK
BOTTLES

Dustproof Stoppered reagents

When ordering your Laboratory requirements be sure to specify Beatson, Clark Dust-Proof Stoppered Reagent Bottles.

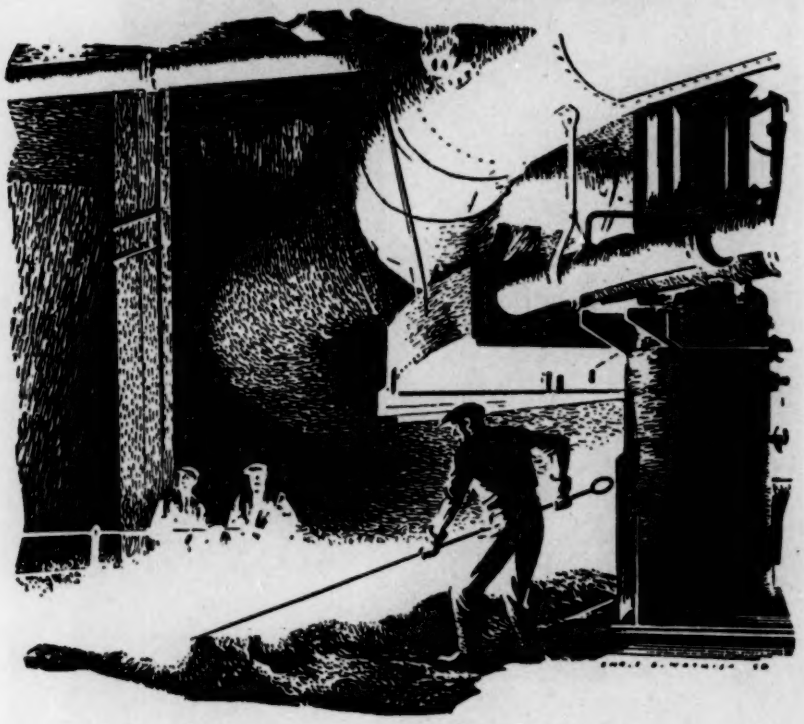
BEATSON, CLARK & CO. LTD.
MANUFACTURERS OF CHEMICAL AND MEDICAL GLASS
ROTHERHAM *Established 1751* **YORKS**

BISOL organic chemicals

BRITISH INDUSTRIAL SOLVENTS LIMITED
4 CAVENDISH SQUARE, LONDON, W.1. Longham 4501

T.A.4001

M&B LABORATORY CHEMICALS
IN THE SERVICE OF INDUSTRY



Away from the toil, heat and noise of the blast furnaces, chemists in the iron and steel industry are unceasingly engaged in performing routine tests on the quality both of raw materials and finished products. In addition, continuous research work is being carried on in an endeavour to produce improved steels for specific purposes.

Many scientists working in the service of the industry have now become accustomed to rely on the high quality of the range of Laboratory Chemicals manufactured by May & Baker. Aware of M&B's long experience in producing all types of fine chemicals, they know they can place their confidence in the specifications which have been drawn up to make these Laboratory Chemicals widely applicable to most kinds of industrial laboratory work.

A complete brochure of specifications will be sent on request.

CH3184

MAY & BAKER LTD. DAGENHAM. Phone: Ilford 3060 Extension 40

AT REIGATE [redacted]

OUR JOB

AS ESSENCE MANUFACTURERS

IS TO TAKE NATURAL PRODUCTS WHICH HAVE A FLAVOUR OR AROMA OR BOTH; EXTRACT FROM THEM THE PRINCIPLES RESPONSIBLE FOR THAT FLAVOUR AND AROMA, AND THEN PREPARE THESE PRINCIPLES IN SUCH A FORM AS TO BE EASILY AND CONVENIENTLY AND ECONOMICALLY USED BY OUR CUSTOMERS.

WE ARE SPECIALISTS IN THIS FIELD AND CAN OFFER GUARANTEED NATURAL PRODUCTS WHICH FOR QUALITY AND TRUE FLAVOUR ARE IN CLASS BY THEMSELVES.

REIGATE BRAND—

VANILLA NATURA
GRAPEFRUIT NATURA
ORANGE NATURA
(SWEET OR BITTER)
ORRIS NATURA

WHITE, TOMKINS & COURAGE, LTD.
NORTH ALBERT WORKS, REIGATE

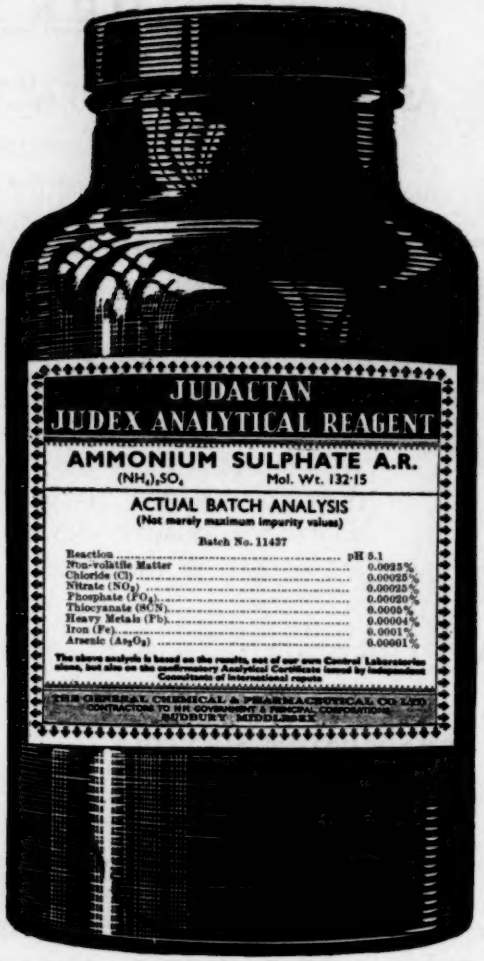
TELEGRAMS: ESSWHITE, REIGATE TELEPHONE: REIGATE 2242-3

ESTABLISHED 1841

JUDACTAN

ANALYTICAL REAGENTS WITH ACTUAL BATCH ANALYSIS

ACTUAL BATCH ANALYSIS


JUDACTAN
JUDEX ANALYTICAL REAGENT
AMMONIUM SULPHATE A.R.
$(NH_4)_2SO_4$ Mol. Wt. 132·15
ACTUAL BATCH ANALYSIS
(Not merely maximum impurity values)
Batch No. 11437
Reaction pH 5.1
Non-volatile Matter 0.0025%
Chlorides (Cl) 0.00025%
Nitrate (NO_3) 0.00025%
Phosphate (PO_4) 0.00020%
Thiocyanate (SCN) 0.0005%
Heavy Metals (Pb) 0.00004%
Iron (Fe) 0.0001%
Arsenic (As_2O_3) 0.00001%
The above analysis is based on the results, not of our own Control Laboratories alone, but also on the confirmatory Analytical Certificate issued by Independent Consultants of international repute.
THE GENERAL CHEMICAL & PHARMACEUTICAL CO. LTD.
CONTRACTORS TO HM GOVERNMENT & PRINCIPAL CORPORATIONS
SUDBURY, MIDDLESEX

Each batch subjected to INDEPENDENT ANALYSIS before label is printed

You are invited to compare the above actual batch analysis with the purities guaranteed by the specifications of any competing maker in this country or abroad.

THE GENERAL CHEMICAL & PHARMACEUTICAL CO. LTD.
Chemical Manufacturers, Judex Works, Sudbury, Middlesex

CONTENTS.

PAPERS COMMUNICATED TO THE CHEMICAL SOCIETY.

General, Physical, and Inorganic.

PAGE

439. The Configuration of Flexible Polymethylene Molecules in the Gas Phase.
By J. C. McCoubrey, J. N. McCrea, and A. R. Ubbelohde 1961

441. The Liquid–Vapour Equilibrium as a Function of Temperature for the System Arsenic Trichloride–Germanium Tetrachloride.
By F. Sebba 1975

446. Trimethylgallium. Part I. The Relative Stabilities of its Co-ordination Compounds with the Methyl Derivatives of Groups Vb and VIb, and the Thermal Decomposition of Some Trimethylgallium–Amine Complexes.
By G. E. Coates 2003

453. Magnetochemistry of the Heaviest Elements. Part IV. Plutonium Trifluoride and Trichloride.
By J. K. Dawson, C. J. Mandleberg, and D. Davies 2047

464. The Alkalimetric Determination of Metals with the Aid of Acid–Base Indicators. Part II.
By J. F. Coetzee 2098

Physical Organic.

437. Theoretical Investigation of Reactivities of Conjugated Bonds. Part II. The Significance of Some Theoretical Quantities.
By R. D. Brown 1950

438. Studies of the Localization Theory of Organic Reactions. Part I. The Effects of Annelation and of Introducing Hetero-atoms.
By R. D. Brown 1955

442. The Probable Existence of Geometrically Isomeric Diazocarboxyamides.
By H. C. Freeman, R. J. W. Le Fèvre, and I. R. Wilson 1977

444. The Kinetics of the Autoxidation of *n*-Decanal. Part I. The Mechanism of Reaction.
By H. R. Cooper and H. W. Melville 1984

445. The Kinetics of the Autoxidation of *n*-Decanal. Part II. The Velocity Constants.
By H. R. Cooper and H. W. Melville 1994

451. The Kinetics of the Dehydrochlorination of Substituted Hydrocarbons. Part VII. The Mechanism of the Thermal Decompositions of 1 : 1 : 2 : 2- and 1 : 1 : 1 : 2-Tetrachloroethane.
By D. H. R. Barton and K. E. Howlett 2033

452. The Kinetics of the Dehydrochlorination of Substituted Hydrocarbons. Part VIII. The Mechanisms of the Thermal Decompositions of *n*-Propyl and *n*-Butyl Chloride and 2 : 2′-Dichlorodiethyl Ether.
By D. H. R. Barton, A. J. Head, and R. J. Williams 2039

465. The Ionisation of Triarylcarbinols in Strong Acids and the Definition of a New Acidity Function.
By V. Gold and B. W. V. Hawes 2102

469. The Determination of Water in Pyridine Homologues by the Use of Infra-red Spectroscopy.
By E. A. Coulson, J. L. Hales, and E. F. G. Herington 2125

Note:

481. The Infra-red Spectra of Three Sydnones and Certain *N*-Nitroso-compounds.
By J. C. Earl, R. J. W. Le Fèvre, A. G. Pulford, and A. Walsh . . 2207

Organic.

435. A New Synthesis of Arsonic Acids. Part I. Coupling of αβ-Unsaturated Carbonyl Compounds with Diazotised *p*-Arsanilic Acid.
By Walter Freund 1943

436. Reduction by Dissolving Metals. Part IX. Some Hydronaphthalene Derivatives.
By A. J. Birch, (Miss) A. R. Murray, and Herchel Smith 1945

PAGE

440. Cinnolines. Part XXVII. The Preparation and Nitration of Cinnoline.
By J. S. MORLEY 1971

443. The Determination of Oxiran-oxygen, with Special Reference to its Application to the Study of Autoxidation.
By GEORGE KING 1980

447. The Chemistry of Fungi. Part XV. The Degradation of Methyl *O*-Dimethylcitromycetin.
By ALEXANDER ROBERTSON, W. B. WHALLEY, and J. YATES 2013

448. Some Alkylresorcinols.
By J. P. BROWN, D. H. JOHNSON, ALEXANDER ROBERTSON, and W. B. WHALLEY 2019

449. Rottlerin. Part VIII. The Rottlerone Change.
By ALEXANDER MCGOOKIN, ALEXANDER ROBERTSON, and T. H. SIMPSON . . 2021

450. The Chemistry of the Melanins. Part III. The Synthesis of Hydroxyindoles from *p*-Benzoquinones.
By R. J. S. BEER, KENNETH CLARKE, H. F. DAVENPORT, and ALEXANDER ROBERTSON 2029

454. The Carbon–Sulphur Fission in Thio-ethers. Part I. The Retarding Influence of α-Methyl Groups and of the Length of the Acid Chain on the Alkaline Hydrolysis of (2-Ketoalkylthio)- and (*p*-Nitrotriphenylmethylthio)-acetic Acids.
By YOUSSEF ISKANDER and RASMY TEWFIK 2050

455. The Carbon–Sulphur Fission in Thio-ethers. Part II. The Retarding Influence of α-Methyl Groups and of the Length of the Acid Chain on the Alkaline Hydrolysis of (Nitrobenzylthio)acetic Acids.
By YOUSSEF ISKANDER and YOUSSEF RIAD 2054

456. The Carbon–Sulphur Fission in Thio-ethers. Part III. The Retarding Influence of the Length of the Radical Chain and of a Second α-Thio-acetic Acid Group on the Alkaline Hydrolysis of (Nitrobenzylthio)- and (Nitrodiphenylmethylthio)-acetic Acids.
By YOUSSEF ISKANDER and ADIB SALAMA 2058

457. Deoxy-sugars. Part XXII. Comparative Rates of Oxidation and Reduction of D-Galactose and 2-Deoxy-D-galactose.
By W. G. OVEREND, F. SHAFIZADEH, and M. STACEY 2062

458. The Synthesis and Reactions of Branched-chain Hydrocarbons. Part I. Hydrocarbons with the 3 : 5 : 5-Trimethylhexyl Group.
By E. M. GUTMAN and W. J. HICKINBOTTOM 2064

459. Purpurogallin. Part VIII. Nitration and Nitrosation of β-Methyltropolone.
By ROBERT D. HAWORTH and PHILLIP R. JEFFERIES 2067

460. New Syntheses of Cystine.
By J. C. CRAWHALL and D. F. ELLIOTT 2071

461. Alkenylation employing Lithium Alkenyls. Part V. The Formation and Some Reactions of *cis*-Propenyl-lithium.
By E. A. BRAUDE and J. A. COLES 2078

462. Studies in Molecular Rearrangement. Part VII. The Oxotropic Rearrangement of *cis*-Propenylcarbinols. The Stereochemical Course of Anionotropy.
By E. A. BRAUDE and J. A. COLES 2085

463. Studies in Molecular Rearrangement. Part VIII. The Five-carbon Oxotropic Rearrangement of 1-Phenylhexa-2 : 4-dien-1-ol.
By H. C. BARANY, E. A. BRAUDE, and J. A. COLES 2093

466. Studies in Peroxidase Action. Part VI. (*a*) The Oxidation of *p*-Anisidine : a Further Example of Ready Demethoxylation. (*b*) Some Theoretical Considerations.
By D. G. H. DANIELS and B. C. SAUNDERS 2112

467. 1 : 8 : 9-Naphthanthr-10-one.
By WILLIAM BRADLEY and F. K. SUTCLIFFE 2118

468. The Addition of Thiolacetic Acid to Unsaturated Compounds.
By R. BROWN, W. E. JONES, and A. R. PINDER 2123

470. Chemistry of Indanthrone. Part I. The Mode of Formation of Indanthrone from 2-Aminoanthraquinone and Potassium Hydroxide.
By WILLIAM BRADLEY and EDWARD LEETE 2129

PAGE

471. Chemistry of Indanthrone. Part II. The Formation of Dianthraquinonyl-*N*-methylamines.
By WILLIAM BRADLEY and EDWARD LEETE 2147

472. Chemistry of Indanthrone. Part III. The Cyclisation of 2-Amino-1 : 2′-dianthraquinonylamine.
By WILLIAM BRADLEY, EDWARD LEETE, and DOUGLAS S. STEPHENS . . 2158

473. Chemistry of Indanthrone. Part IV. An Isomer of Indanthrone and the Constitution of Indanthren B.
By WILLIAM BRADLEY, EDWARD LEETE, and DOUGLAS S. STEPHENS . . 2163

474. Chemistry of Indanthrone. Part V. *tert.*-Butyl Derivatives of Indanthrone and Flavanthrone. The Mode of Formation of Flavanthrone in the Alkali Fusion of 2-Aminoanthraquinone.
By WILLIAM BRADLEY and HARRY E. NURSTEN 2170

475. Chemistry of Indanthrone. Part VI. Alkylsulphonylindanthrones.
By WILLIAM BRADLEY and HARRY E. NURSTEN 2177

476. Dimethin*mero*cyanines derived from 2-Substituted Azol-5-ones.
By PER AUBERT, E. B. KNOTT, and L. A. WILLIAMS 2185

477. Thiazolid-2 : 5-dione.
By PER AUBERT, R. A. JEFFREYS, and E. B. KNOTT 2195

478. The Separation of Acids by Paper Partition Chromatography.
By A. G. LONG, J. R. QUAYLE, and R. J. STEDMAN 2197

479. Compounds related to Thiosemicarbazide. Part VIII. The Oxidation of Thiosemicarbazones.
By ERIC HOGGARTH 2202

480. The Synthesis of 1-Substituted Phosphindolines.
By FREDERICK G. MANN and IAN T. MILLAR 2205

NOTES :

482. Trichloromethylamine (Aminochloroform).
By K. R. SIMON ASCHER 2209

483. The Reaction of Aromatic Hydrocarbons with Lithium Aluminium Hydride, and a New Technique for the Use of the Reagent.
By ISAAC GOODMAN 2209

484. The Dehydration of 6β-Acetoxy-3β-methoxycholestan-5α-ol.
By M. DAVIS and V. PETROW 2211

485. The Formation of Osazones. Part III.
By G. J. BLOINK and K. H. PAUSACKER 2212

486. The Bromination of *o*-Acylaminotoluenes. A Correction.
By D. G. I. FELTON 2213

487. A New Synthesis of 4 : 6-Dihydroxypyrimidines.
By R. HULL 2214

INDEX OF AUTHORS' NAMES.

Ascher, K. R. S., 2209.
Aubert, P., Jeffreys, R. A., and Knott, E. B., 2195.
Aubert, P., Knott, E. B., and Williams, L. A., 2185.
Barany, H. C., Braude, E. A., and Coles, J. A., 2093.
Barton, D. H. R., Head, A. J., and Williams, R. J., 2039.
Barton, D. H. R., and Howlett, K. E., 2033.
Beer, R. J. S., Clarke, K., Davenport, H. F., and Robertson, A., 2029.
Birch, A. J., Murray, A. R., and Smith, H., 1945.
Bloink, G. J., and Pausacker, K. H., 2212.
Bradley, W., and Leete, E., 2129, 2147.
Bradley, W., Leete, E., and Stephens, D. S., 2158, 2163.
Bradley, W., and Nursten, H. E., 2170, 2177.
Bradley, W., and Sutcliffe, F. K., 2118.
Braude, E. A., and Coles, J. A., 2078, 2085.
Braude, E. A. See also Barany, H. C., 2093.
Brown, J. P., Johnson, D. H., Robertson, A., and Whalley, W. B., 2019.
Brown, R., Jones, W. E., and Pinder, A. R., 2123.
Brown, R. D., 1950, 1955.
Clarke, K. See Beer, R. J. S., 2029.
Coates, G. E., 2003.
Coetzee, J. F., 2098.
Coles, J. A. See Barany, H. C., 2093, and Braude, E. A., 2078, 2085.
Cooper, H. R., and Melville, H. W., 1984, 1994.
Coulson, E. A., Hales, J. L., and Herington, E. F. G., 2125.
Crawhall, J. C., and Elliott, D. F., 2071.
Daniels, D. G. H., and Saunders, B. C., 2112.
Davenport, H. F. See Beer, R. J. S., 2029.
Davies, D. See Dawson, J. K., 2047.
Davis, M., and Petrow, V., 2211.
Dawson, J. K., Mandelberg, C. J., and Davies, D., 2047.
Earl, J. C., Le Fèvre, R. J. W., Pulford, A. G., and Walsh, A., 2207.
Elliott, D. F. See Crawhall, J. C., 2071.
Felton, D. G. I., 2213.
Freeman, H. C., Le Fèvre, R. J. W., and Wilson, I. R., 1977.
Freund, W., 1943.
Gold, V., and Hawes, B. W. V., 2102.
Goodman, I., 2209.
Gutman, E. M., and Hickinbottom, W. J., 2064.
Hales, J. L. See Coulson, E. A., 2125.
Hawes, B. W. V. See Gold, V., 2102.
Haworth, R. D., and Jefferies, P. R., 2067.
Head, A. J. See Barton, D. H. R., 2039.
Herington, E. F. G. See Coulson, E. A., 2125.
Hickinbottom, W. J. See Gutman, E. M., 2064.
Hoggarth, E., 2202.
Howlett, K. E. See Barton, D. H. R., 2033.
Hull, R., 2214.
Iskander, Y., and Riad, Y., 2054.
Iskander, Y., and Salama, A., 2058.
Iskander, Y., and Tewfik, R., 2050.
Jefferies, P. R. See Haworth, R. D., 2067.
Jeffreys, R. A. See Aubert, P., 2195.
Johnson, D. H. See Brown, J. P., 2019.
Jones, W. E. See Brown, R., 2123.
King, G., 1980.
Knott, E. B., See Aubert, P., 2185, 2195.
Leete, E. See Bradley, W., 2129, 2147, 2158, 2163.
Le Fèvre, R. J. W. See Earl, J. C., 2207, and Freeman, H. C., 1977.
Long, A. G., Quayle, J. R., and Stedman, R. J., 2197.
McCoubrey, J. C., McCrea, J. N., and Ubbelohde, A. R., 1961.
McCrea, J. N. See McCoubrey, J. C., 1961.
McGookin, A., Robertson, A., and Simpson, T. H., 2021.
Mandelberg, C. J. See Dawson, J. K., 2047.
Mann, F. G., and Millar, I. T., 2205.
Melville, H. W. See Cooper, H. R., 1984, 1994.
Millar, I. T. See Mann, F. G., 2205.
Morley, J. S., 1971.
Murray, A. R. See Birch, A. J., 1945.
Nursten, H. E. See Bradley, W., 2170, 2177.
Overend, W. G., Shafizadeh, F., and Stacey, M., 2062.
Pausacker, K. H. See Bloink, G. J., 2212.
Petrow, V. See Davis, M., 2211.
Pinder, A. R. See Brown, R., 2123.
Pulford, A. G. See Earl, J. C., 2207.
Quayle, J. R. See Long, A. G., 2197.
Riad, Y. See Iskander, Y., 2054.
Robertson, A., Whalley, W. B., and Yates, J., 2013.
Robertson, A. See also Beer, R. J. S., 2029, Brown, J. P., 2019, and McGookin, A., 2021.
Salama, A. See Iskander, Y., 2058.
Saunders, B. C. See Daniels, D. G. H., 2112.
Sebba, F., 1975.
Shafizadeh, F. See Overend, W. G., 2062.
Simpson, T. H. See McGookin, A., 2021.
Smith, H. See Birch, A. J., 1945.
Stacey, M. See Overend, W. G., 2062.
Stedman, R. J. See Long, A. G., 2197.
Stephens, D. S. See Bradley, W., 2158, 2163.
Sutcliffe, F. K. See Bradley, W., 2118.
Tewfik, R. See Iskander, Y., 2050.
Ubbelohde, A. R. See McCoubrey, J. C., 1961.
Walsh, A. See Earl, J. C., 2207.
Whalley, W. B. See Brown, J. P., 2019, and Robertson, A., 2013.
Williams, L. A. See Aubert, P., 2185.
Williams, R. J. See Barton, D. H. R., 2039.
Wilson, I. R. See Freeman, H. C., 1977.
Yates, J. See Robertson, A., 2013.

NOTICES TO AUTHORS OF PAPERS

SUBMISSION OF PAPERS. 1. Scientific Communications for the *Journal* should be addressed to "The Honorary Secretaries, The Chemical Society, Burlington House, London, W.1." Papers to be read before a meeting of the Society are selected by the Honorary Secretaries.

2. A paper is not normally considered for publication in the *Journal* unless at least one of the authors is a Fellow of the Society, but in exceptional circumstances the Council is prepared to consider papers submitted by non-Fellows.

3. Communications which have appeared or have been accepted for publication with essentially the same scientific content in another Journal or freely available printed work shall not be published in the *Journal* of the Society unless this course is approved by the Council.

4. Papers are accepted by the Society on the understanding that the authors have obtained any necessary authority to publish.

5. The Society reserves the right to retain all papers sent to it, and authors are therefore advised to keep copies. When papers have been accepted for publication the authors are not at liberty, save by permission of the Council, to withdraw or delay them, or to publish them elsewhere until they have appeared in the *Journal* of the Society. Papers which are retained by the Council after being judged unsuitable for publication in the *Journal* are deposited in the Archives of the Society; this right is not usually exercised in regard to illustrations.

MANUSCRIPT. 6. All manuscripts must be top copies, clearly typed, on non-absorbent paper, in double-line spacing and on one side only.

7. The address to which proofs are to be sent must be given on the front page of every paper.

RESPONSIBILITY. 8. Authors are solely responsible for the factual accuracy of their papers. They are particularly requested to verify references and to indicate positions of cross-references.

SUMMARY. 9. Every paper must be prefaced by a short summary (50—250 words) setting forth briefly and in simple language the objects of the investigation and the results obtained. The summary should give any chemist a clear idea of what the investigation has achieved and should be independent of the main text. "Notes" do not require a summary.

STYLE. 10. Authors are requested to see that their papers conform, as nearly as possible, to the normal style, conventions, and conciseness of the *Journal*.

NOMENCLATURE. 11. Authors are expected to be familiar with the normal rules of nomenclature, but are invited to communicate with the Editor if in doubt or in special cases. Some of the principles followed in the *Journal* are reviewed in "Modern Chemical Nomenclature," by Dr. Clarence Smith (*J.*, 1936, 1067) (6*d.* post free), and in the Editorial Report on Nomenclature, 1950 (*J.*, 1950, 3699) (1*s.* post free). Much valuable discussion will be found in "British Chemical Nomenclature," by Dr. A. D. Mitchell [Edward Arnold & Co., 1948]. Authors should choose their symbols from the "Report by the Symbols Committee of the Royal Society representing the Royal Society, the Chemical Society, the Faraday Society, and the Physical Society, 1951" (*J.*, 1951, 1677) [9*d.* per copy or 12*s.* per 25 copies (post free)].

NEW COMPOUNDS. 12. New compounds should be indicated by underlining the name at its first mention (excluding headings) in the Experimental section *only*, and by giving analytical results in the form: "Found: ———. ——— requires ———." Analytical results for compounds which have previously been adequately described in the literature should be given in the form: "Found: ———. Calc. for ———. ———."

ILLUSTRATIONS. 13. Illustrations accompanying the papers must be carefully drawn, preferably *twice* the size of the finished block (max. width 5 inches), *in Indian ink, on good white cartridge paper* (graph paper with faint blue lines is acceptable). Any illustration which seriously exceeds four times the size of the finished block will be returned to the author for re-drawing to a smaller scale. Lettering on the drawings, whether on the margin or in the body of the drawing, must not be in ink but must be inserted *clearly but lightly in pencil*. *Margins* of at least two inches must be left. Authors may, if they wish, submit in the first place clearly drawn pencil sketches instead of the completed diagrams, which, however, must be supplied before publication. Further information can be obtained from the Editor.

PROOFS. 14. Authors will be expected to pay the cost of any considerable changes made by them in proof, apart from the correction of printers' errors. See also paragraph 7.

PREPRINTS. 15. Each author, or joint author, receives 10 preprints (without covers) free of charge. A quotation for extra preprints and an order form will be sent with the proofs. The order form (and any necessary remittance) must be returned with the proofs.

INFORMATION FOR CANDIDATES FOR FELLOWSHIP

The Chemical Society was founded in 1841 and received a Royal Charter in 1848.

The main function of the Society is to foster original research in chemistry and to facilitate the discussion and dissemination of new knowledge in all branches of the science.

Fellowship of the Society is open to men and women of all nationalities who are interested in chemistry and wish to keep in touch with its advances. Fellows are elected by the Council.

PRIVILEGES

Fellows who pay the annual subscription of £3 10*s*. have the following privileges.

1. To receive a selection of the Society's publications. Publications in excess of those allowed under the Annual Subscription may be purchased at favourable rates.

   Details are available on application to the General Secretary.

2. To consult and borrow the books in the Library.
3. To attend meetings of the Society both in London and outside London, and to introduce two guests thereto.
4. To apply for research grants.
5. To submit original papers for publication in the *Journal*.

Fellows under the age of 25, who so wish, may pay an annual subscription of £1 15*s*. and enjoy all the privileges accorded to those paying the full subscription except that the choice of publications is limited.

PUBLICATIONS

(*a*) *The Journal of the Chemical Society*, which is published monthly, contains the results of investigations which cover the whole field of pure chemistry.

(*b*) *British Abstracts*.—The Society collaborates with the Society of Chemical Industry, the Physiological Society, the Biochemical Society, and other organisations in contributing to the maintenance of the Bureau of Abstracts, which issues every month abstracts of papers dealing with all branches of pure and applied chemistry, physiology, and anatomy published in all parts of the world.

British Abstracts A is divided into three sections: AI, General, Physical, and Inorganic Chemistry; AII, Organic Chemistry; AIII, Physiology and Biochemistry, including Anatomy.

(*c*) *Annual Reports on the Progress of Chemistry*.—These reports, written by experts, summarise the important new advances in pure chemistry and related subjects.

(*d*) *Quarterly Reviews* are composed of articles on selected topics from the whole field of chemistry.

LIBRARY

The extensive reference and lending library of the Chemical Society contains over 47,000 volumes dealing with every aspect of chemistry and with many branches of related sciences. The library is open on Monday to Friday from 10 a.m. to 9 p.m., and on Saturdays from 10 a.m. to 5 p.m.

Books available on loan may be sent by post to Fellows residing in Great Britain or Ireland.

MEETINGS

(*a*) *In London*.—Scientific Meetings of the Society are held usually on the first and third Thursdays of each month from October to June at Burlington House, at which papers dealing with original work are read and discussed, organised discussions on subjects of current interest are arranged, and lectures by eminent British and foreign chemists are delivered.

(*b*) *Outside London*.—Scientific Meetings and lectures arranged by the Society's Local Representatives are also held outside London, and form an important part of the activities of the Society.

RESEARCH FUND

A Research Fund is available for the assistance of chemical research, and sums amounting annually to about £700 are granted for this purpose. Application for grants must be made on the appropriate form, which may be obtained from the General Secretary.

Forms of Application for Fellowship can be obtained from THE GENERAL SECRETARY, THE CHEMICAL SOCIETY, BURLINGTON HOUSE, PICCADILLY, LONDON, W.1.

435. *A New Synthesis of Arsonic Acids. Part I. Coupling of αβ-Unsaturated Carbonyl Compounds with Diazotised* p-*Arsanilic Acid.*

By Walter Freund.

Arsonic acids can be synthesised by treating diazotised *p*-arsanilic acid with appropriate compounds in such a way that nitrogen is split off. The arsonophenyl group reacts with the α-carbon atom of cinnamic acids and coumarin, yielding 4-arsonostilbenes and 3-*p*-arsonophenylcoumarin.

For the preparation of aromatic arsonic acids three methods are available: the Béchamp (*Compt. rend.*, 1863, **56**, 1172), the Bart (D.R.-P. 250,264/1910; *Zentr.*, 1912, II, 882), and the Rosenmund (*Ber.*, 1921, **54**, 438) process. It has now been found that diazotised arsanilic acids, *e.g.*, diazotised *p*-arsanilic acid, can under appropriate conditions be coupled with a variety of compounds in such a way that nitrogen is split off and a new arsonic acid is formed (Austral. P. 18758/1948).

It is generally assumed that by the decomposition of a diazo-compound an organic radical is formed which stabilises itself by becoming attached to another carbon atom. The reaction was first reported by Möhlau and Berger (*Ber.*, 1893, **26**, 1994), Kühling (*Ber.*, 1895, **28**, 41, 523), and Bamberger (*ibid.*, p. 403) and is usually carried out in alkaline solution.

In 1939 Meerwein, Buchner, and van Emster (*J. pr. Chem.*, **152**, 237; B.P. 480,617) described a method of arylating αβ-unsaturated carbonyl compounds by treating them with diazotised amines in weakly acidic aqueous acetone, with cupric chloride as a catalyst. This method has been adapted to introduce the phenylarsonic acid group into other molecules. As the new arsonic acid (*e.g.*, stilbene-4-arsonic acid from diazotised *p*-arsanilic acid and cinnamic acid) separates as a copper salt or copper complex salt, the cupric chloride is used up during the reaction. The formation of such salts facilitates the isolation of the arsonic acids. The yields are only moderate, approximately 30%, sometimes much smaller, but no efforts have so far been made to find out optimum conditions. The success of the reaction depends to a large extent on the particular unsaturated compound used for coupling. As observed by Meerwein *et al.* (*loc. cit.*) aromatic amines having an electronegative substituent in the *para*-position are the best arylating agents. *p*-Arsanilic acid couples well, but is somewhat inferior to *p*-nitroaniline or *p*-chloroaniline. *m*-Arsanilic acid gives lower yields, and *o*-arsanilic acid has so far failed to yield any arylation products.

Coupling of cinnamic or substituted cinnamic acid yields 4-arsonostilbenes. On the other hand, *p*-methoxycinnamic acid does not lose carbon dioxide during the reaction, the product being α-*p*-arsonophenyl-β-*p*-methoxyphenylacrylic acid. Coumarin yields 3-*p*-arsonophenylcoumarin.

A side-reaction met with in the decomposition of diazo-compounds is the formation of symmetrical azo-compounds. In the Meerwein reaction the formation of symmetrical azo-compounds has been observed only when the reaction between the diazo-compound and the αβ-unsaturated carbonyl compound is unsatisfactory (Meerwein *et al.*, *loc. cit.*). In the case of diazotised *p*-arsanilic acid, azobenzene-*pp'*-diarsonic acid is obtained if the evolution of nitrogen is slow. When the reaction is very slow, *e.g.*, when *p*-arsanilic acid reacts with 4-hydroxy-3-nitrocinnamic acid, the azobenzene-*pp'*-diarsonic acid may become the chief product.

The reaction has been extended to compounds such as furan, thiophen, furylacrylic acid, ω-2-furylheptatrienoic acid, and thienylacrylic acid; the results will be reported later.

Experimental.

Stilbene-4-arsonic Acid.—*p*-Arsanilic acid (21·7 g.), dissolved in a solution of sodium hydroxide (4·2 g.) in water (*ca.* 200 c.c.), was mixed with a solution of sodium nitrite (7·3 g.) in water (20 c.c.) and diazotised with 25% hydrochloric acid (60 g.) in the usual manner. The diazotised solution was then added to a solution of cinnamic acid (14·8 g.) in acetone (200 c.c.) in which approx. 70 g. of crystallised sodium acetate were suspended. The mixture was well shaken or stirred until the pH becomes adjusted to approx. 6. A solution of cupric chloride (20 g.) in water (45 c.c.) was added dropwise during 3—4 hours and the whole warmed gently on a water-bath to start gas evolution. The product separated as a buff-colour copper salt. When gas evolution ceased, the precipitate was allowed to settle, the supernatant liquid was decanted, and the precipitate twice agitated with 100—150 c.c. of acetone to remove unchanged cinnamic acid. These acetone washings were mixed with the first decanted mother-liquor from which by conventional methods some cinnamic acid could be recovered. The

precipitate was then collected and air-dried. The dried material was digested with approx. 2N-sodium hydroxide in which the new arsonic acid was easily soluble, the copper being precipitated. After filtration, the alkaline solution was acidified with hydrochloric acid, giving the arsonic acid as a light yellowish solid which was finally dried in a desiccator. *Stilbene-4-arsonic acid* recrystallised from acetic acid, from which buff-coloured plates (30—35%) separated which did not melt at 300° (Found: C, 55·1, 55·0; H, 4·4, 4·3; As, 24·8. $C_{14}H_{13}O_3As$ requires C, 55·3; H, 4·3; As, 24·6%).

4'-Methylstilbene-4-arsonic Acid.—*p*-Arsanilic acid (10·85 g.) in N-sodium hydroxide (60 c.c.) was treated with sodium nitrite (3·65 g.) in water (10 c.c.), and the whole added with cooling to hydrochloric acid (30—32 c.c.). The clear diazo-solution was added to 4-methylcinnamic acid (8·1 g.) in acetone (approx. 220 c.c.) in which 20 g. of cryst. sodium acetate were suspended. Gas evolution set in only after some cupric chloride (altogether 10 g., in 22 c.c. of water) had been added. The gas evolution was good at 30—35° and lasted for about 0·5 hour during which the cupric chloride solution was added dropwise. A buff-coloured solid separated and was filtered off and washed with acetone (100 c.c.). The air-dried material was dissolved in 2N-sodium hydroxide. The reddish-brown solution was filtered and the filtrate treated with hydrochloric acid. The precipitate was dried in a vacuum-desiccator (yield, 4·9 g., 30%). *4'-Methylstilbene-4-arsonic acid* separated from acetic acid in slightly yellowish plates which did not melt at 300° (Found: C, 56·6, 56·5; H, 4·8, 4·8; As, 23·7. $C_{15}H_{15}O_3As$ requires C, 56·65; H, 4·7; As, 23·6%).

From the acetone–water mother-liquors 4·5 g. of 4-methylcinnamic acid were recovered.

4'-Hydroxystilbene-4-arsonic Acid.—*p*-Arsanilic acid (10·85 g.) was diazotised as above and added to a solution of *p*-hydroxycinnamic acid (8·2 g.) in acetone (120 c.c.) to which 0·3 mole of sodium chloroacetate in a little water had been added as buffer. Gas evolution set in immediately. Cupric chloride (10 g.) in water (20—22 c.c.) was added in small portions. The gas evolution lasted for approx. 40 minutes at 22°. The solid which separated was worked up in the usual way. The arsonic acid which was obtained contained nitrogenous material. It was digested with cold sodium hydrogen carbonate solution which dissolved some dark material (azobenzene-*pp'*-diarsonic acid). *4'-Hydroxystilbene-4-arsonic acid* (*ca.* 5 g.) remained undissolved in the alkaline solution. Recrystallisation from acetic acid gave slightly yellowish plates which did not melt at 300°. The material was free from nitrogen (Found: C, 52·5, 52·3; H, 4·1, 4·1; As, 23·5. $C_{14}H_{13}O_4As$ requires C, 52·5; H, 4·1; As, 23·4%). The material soluble in cold sodium hydrogen carbonate was dried on porous tile, extracted with cold alcohol, and recrystallised from acetic acid in which it is sparingly soluble with a red colour. Dark, poorly developed crystals of azobenzene-*pp'*-diarsonic acid were obtained which did not melt at 300° (Found: C, 33·4, 33·4; H, 2·9, 3·0; N, 6·5; As, 35·1. Calc. for $C_{12}H_{12}O_6N_2As_2$: C, 33·5; H, 2·8; N, 6·5; As, 34·85%) (cf. Karrer, *Ber.*, 1912, **45**, 2362; Fichter and Elkind, *Ber.*, 1916, **49**, 246).

4-Arsono-α-cyanostilbene.—Coupling of diazotised *p*-arsanilic acid with cinnamonitrile yielded *4-arsono-α-cyanostilbene* (*ca.* 20%), slightly yellowish plates and needles (from alcohol), which did not melt at 300° (Found: C, 54·6, 54·6; H, 3·5, 3·8; N, 4·1, 4·0. $C_{15}H_{12}O_3NAs$ requires C, 54·7; H, 3·65; N, 4·3; As, 22·8%).

4-Arsono-4'-methoxystilbene-α-carboxylic Acid.—Coupling of diazotised *p*-arsanilic acid with *p*-methoxycinnamic acid yielded this *acid* (*ca.* 20%) which crystallised from acetic acid in small nearly white plates which did not melt at 300° (Found: C, 51·1 51·25; H, 4·2, 4·2; As, 19·35; MeO, 7·9, 7·95. $C_{16}H_{15}O_6As$ requires C, 50·8; H, 3·9; As, 19·8; MeO, 8·2%).

3-p-Arsonophenylcoumarin.—The reaction was carried out as described in previous examples, the yield being approx. 55%. The *coumarin* crystallised from acetic acid in slightly yellowish plates which did not melt at 300° (Found: C, 51·9, 52·1; H, 3·3, 3·35; As, 21·6. $C_{15}H_{11}O_5As$ requires C, 52·0; H, 3·2; As, 21·45%).

I thank Dr. K. F. Tettweiler, formerly of the University of Melbourne, for the analyses. This work was supported in part by a grant from the National Council for Health and Medical Research, Canberra.

Department of Physiology, The University, Melbourne. [*Received, January 4th*, 1950.]

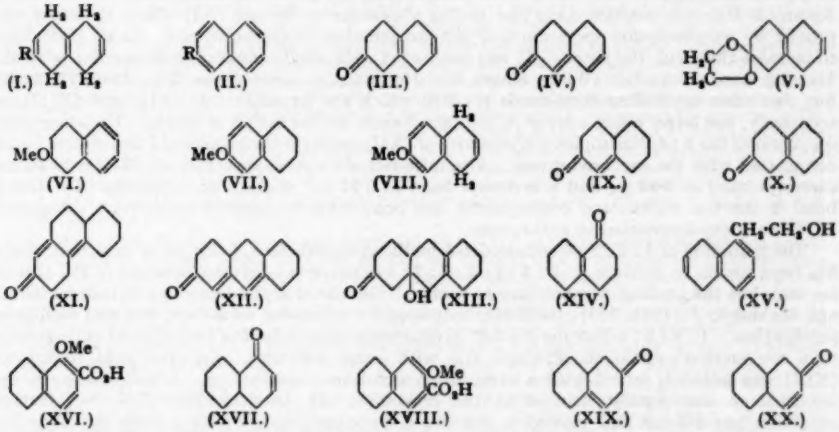
436. *Reduction by Dissolving Metals. Part IX.* Some Hydronaphthalene Derivatives.*

By A. J. Birch, (Miss) A. R. Murray, and Herchel Smith.

In connection with work on the synthesis of polycyclic hydroaromatic compounds related to the steroids some naphthalene and tetrahydronaphthalene derivatives have been reduced with sodium and alcohols in liquid ammonia to give a number of new tetra- and hexa-hydronaphthalene derivatives. Those carrying a methoxy- or 2-hydroxyethoxy-group attached to the dihydrobenzene ring have been hydrolysed by acids to hydronaphthyl ketones, of which (X) reacts by the Robinson–Mannich procedure to give a decahydroketophenanthrene.

Work in progress on polycyclic hydroaromatic compounds has made necessary an investigation of the partial reduction of benzenoid compounds containing more than one ring. The present communication reports some reductions of naphthalene and partly hydrogenated naphthalene derivatives by means of sodium and methanol or ethanol in liquid ammonia, with the principal object of preparing hydronaphthyl ketones as intermediates for further synthesis and as model compounds.

Naphthalene itself can be readily reduced to a crystalline tetrahydro-derivative which is probably 1 : 4 : 5 : 8-tetrahydronaphthalene (I; R = H). The double bonds are not conjugated because if this were so reduction would not stop at the tetrahydro-stage; furthermore, the substance possesses no light-absorption maximum in the region 2200—2800 A. 2-Methoxy- and 2-2′-hydroxyethoxy-naphthalene (II; R = OMe or O·CH$_2$·CH$_2$·OH) can similarly be



reduced to what are probably the 1 : 4 : 5 : 8-tetrahydro-derivatives (I; R = OMe or O·CH$_2$·CH$_2$·OH). Careful hydrolysis of (I; R = O·CH$_2$·CH$_2$·OH) by dilute acid gave rise to the $\beta\gamma$-unsaturated ketone (III) which has no significant absorption in the region 2200—2800 A. and gives rise to an orange 2 : 4-dinitrophenylhydrazone converted by acid into the dark red derivative of (IV). The ketone (IV) could be obtained directly from (I; R = OMe) by more vigorous acid hydrolysis and possesses a maximum at 2800 A. which is indicative of two double bonds conjugated with the carbonyl group (Evans and Gillam, *J.*, 1945, 432). The action of a trace of toluene-*p*-sulphonic acid on (I; R = O·CH$_2$·CH$_2$·OH) produced a rise in temperature and formation of an isomeric substance, of lower boiling point and viscosity, which is formulated as the cyclic ketal (V) since it gave rise to the derivative of (III) by the action of Brady's reagent in the cold.

* Part VIII, *J. Proc. Roy. Soc., N.S.W.*, 1950, **83**, 245.

αδ-Dihydrobenzene derivatives often disproportionate in the presence of hydrogenation catalysts (*e.g.*, γ-terpinene; Richter and Wolff, *Ber.*, 1930, **63**, 1721), and the action of Raney nickel on (I; R = OMe) was examined in the hope of obtaining a worthwhile yield of (VII). The reaction proceeded exothermally in ethanol, but the product contained about 15% of 2-methoxynaphthalene in addition to 25% of (VI) and 35% of (VII). The reaction is therefore of no practical importance for the preparation of the last substance, but is of interest in connection with the mechanism of the catalytic hydrogenation of naphthalenes, since it is evident that if compounds of the type (I) are intermediates in this process they will not long survive as such.

The preparation in good yield of 1 : 4-dihydro-6-methoxynaphthalene (VIII) would be of interest because 2-methoxynaphthalene normally is reduced in the substituted ring (Cornforth, Cornforth, and Robinson, *J.*, 1942, 689; Beer, D.Phil. Thesis, Oxford, 1948). An attempt was made to prepare it from (I; R = OMe) by partial oxidation with lead tetra-acetate (cf. Birch, *J.*, 1950, 1551). There seemed reason to expect that the methoxy-containing ring would be oxidised the more readily since an intermediate radical or cation formed by removal of $H^{\cdot}$ or H^{+} would probably be stabilised by an adjacent methoxyl group. With one mol. of lead tetra-acetate a 20% yield of (VIII) was proved by formation of the crystalline dibromide (cf. Beer, *loc. cit.*) accompanied by only a trace of the isomeric 2 : 5-dihydro-2-methoxynaphthalene. 2-Methoxynaphthalene was also formed. It seems probable that the use of a milder oxidising agent should give a better yield of (VIII), but interest in the process has diminished with the discovery that the B-ring of compounds of the equilenin type cannot be reduced by the metal–ammonia method (Birch and Smith, *J.*, 1951, 1882) and consequently the process would be useless for converting equilenin into equilin.

The reduction of 1 : 2 : 3 : 4-tetrahydro-6-methoxynaphthalene (VII) has already been briefly reported (Birch, *J.*, 1944, 430), the product identified after vigorous acid hydrolysis being (IX). Milder conditions have now been found to give (X), which, unlike (IX), gives rise to a bisulphite compound. The double bond shows a surprising stability in the βγ-position, and the Robinson–Mannich reaction gave rise to the phenanthrene ketone (XI) whose structure was proved by its absorption spectrum and dehydrogenation to phenanthrene. In an endeavour to increase the yield, the ketone (X) was condensed with ethyl formate before reaction with the Mannich base methiodide (Wilds, Shunk, and Hoffman, *J. Amer. Chem. Soc.*, 1949, **71**, 3266), but two other crystalline compounds resulted which are formulated as (XII) and (XIII) respectively, the latter being converted into the former by the action of alkali. The absorption spectrum of the 2 : 4-dinitrophenylhydrazone of (XII) confirms the presence of two double bonds conjugated with the carbonyl group. The infra-red absorption spectrum of (XIII) shows the carbonyl band at 5·82 μ., and a hydroxyl band at 2·97 μ.; there is no indication of a double bond in the 6-μ. region, and consequently this bond must be situated as shown. Compound (XII) was dehydrogenated to anthracene.

The reduction of 1 : 2 : 3 : 4-tetrahydro-5-methoxynaphthalene, followed by acid hydrolysis, has been shown to produce 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-octahydro-1-ketonaphthalene (XIV) (Birch, *loc. cit.*), but the product was not easy to purify. The use of aryl 2-hydroxyethyl ethers (Birch and Mukherji, *J.*, 1949, 2531) facilitates reduction by increasing solubility, and also facilitates purification. 1 : 2 : 3 : 4-Tetrahydro-5-2′-hydroxyethoxynaphthalene was reduced more readily than the methoxy-analogue, although still with some difficulty, and after acid hydrolysis (XIV) was isolated, mixed with a little decahydro-1-ketonaphthalene. 1-2′-Hydroxyethoxynaphthalene was readily reduced to the crystalline dihydro-derivative (XV), but further reduction was difficult and yielded a mixture of hydrocarbons containing some (I; R = H), together with material which on acid hydrolysis formed a mixture of ketones.

Double bonds in positions different from those found in the products of direct reduction would result if reduction could be forced to occur in positions carrying a saturated carbon atom. In order to do this an electron-attracting group must be present which has a more powerful orientating influence than that of the electron-repelling saturated substituent; a group which is, moreover, readily removed if necessary. The most obvious one is carboxyl, which, if *ortho* to the alkoxy-group, can be eliminated by decarboxylation after acid hydrolysis to a β-keto-acid. The Kolbe reaction on 1 : 2 : 3 : 4-tetrahydro-5- and -6-hydroxynaphthalene, followed by methylation with a very large excess of methyl sulphate produced the acids (XVI) and (XVIII) which were reduced with sodium and ethanol in ammonia. From (XVI) was obtained, after acid hydrolysis and removal of the acidic fraction, a poor yield of a crystalline ketone (XVII), and from (XVIII) a poor yield of a mixture of ketones probably (XIX) and (XX). In both cases the preponderant product was acidic, and was not closely examined. That from

(XVI) was found to produce by the action of chromic acid a high yield of 1 : 2 : 3 : 4-tetrahydro-6-naphthoic acid, and probably consists essentially of 2 : 5 : 6 : 7 : 8 : 10-hexahydro-2-naphthoic acid produced by removal of methoxyl and reduction of the ring. This process is known to occur to a large extent with *o*- and *p*-anisic acid. The yields of ketone were too small for practical application, although compounds not accessible by other means were produced. The reduction of some other polycyclic systems is being examined.

Experimental.

1 : 4 : 5 : 8-*Tetrahydronaphthalene* (I; R = H).—Naphthalene (10 g.) in ethanol (40 c.c.) and ether (50 c.c.) was added rapidly to liquid ammonia (250 c.c.), with rapid stirring to give a fine precipitate. Sodium (15 g.) was added in small pieces, the reacion being at first very vigorous. Water (200 c.c.) was then added, and the solid removed by filtration, well washed with water, dried, and crystallised from methanol. 1 : 4 : 5 : 8-*Tetrahydronaphthalene* so obtained formed large plates (6·2 g.), m. p. 42° (Found : C, 87·1; H, 12·6. $C_{9}H_{14}$ requires C, 87·3; H, 12·7%). It resembled naphthalene in appearance, but the odour was fainter and more pleasant; it failed to give adducts with picric acid or trinitrobenzene, and rapidly became brown and sticky in air.

1 : 4 : 5 : 8-*Tetrahydro-2-methoxynaphthalene* (I; R = OMe).—2-Methoxynaphthalene (7 g.) in warm ethanol (25 c.c.) was stirred into ammonia (300 c.c.) and reduced with sodium (7 g.). After working up in the usual manner, distillation gave 1 : 4 : 5 : 8-*tetrahydro-2-methoxynaphthalene* as an oil, b. p. 128°/10 mm., 136—137°/17 mm. (5·8 g.) (Found : C, 81·0; H, 8·8. $C_{11}H_{14}O$ requires C, 81·4; H, 8·6%). Hydrolysis by refluxing sulphuric acid (5%) for 2 hours, and distillation gave 2 : 3 : 4 : 5 : 6 : 10-*hexahydro-2-ketonaphthalene*, b. p. 137—140°/12 mm. (4·4 g.), $\lambda_{max.}$ 2800 A. (ε 14,800) (Found : C, 80·9; H, 8·4. $C_{10}H_{14}O$ requires C, 81·0; H, 8·1%). It gave a derivative with Brady's reagent as purple-red needles (from ethyl acetate), m. p. 202°, and a *semicarbazone* as cream-coloured prisms (from ethanol), m. p. 210—212° (Found : C, 64·0; H, 7·3. $C_{11}H_{18}ON_{3}$ requires C, 64·4; H, 7·3%).

1 : 4 : 5 : 8-*Tetrahydro-2-2′-hydroxyethoxynaphthalene*.—2-2′-Hydroxyethoxynaphthalene was prepared in the standard manner from β-naphthol and ethylene chlorohydrin in hot aqueous sodium hydroxide and had m. p. 63°, although Harnack (*J. Amer. Chem. Soc.*, 1920, **42**, 164) gives m. p. 76—77°. The naphthalene derivative (19 g.) in methanol (60 c.c.) was added to ammonia (500 c.c.), followed by sodium (21 g.) during 30 minutes with stirring. When reaction was complete, water (200 c.c.) was added, and the product extracted with ether and distilled, to give 1 : 4 : 5 : 8-*tetrahydro-2-2′-hydroxyethoxynaphthalene* (12 g.), b. p. 156—157°/1 mm., m. p. 65° (Found : C, 74·6; H, 8·5. $C_{12}H_{16}O_{2}$ requires C, 75·0; H, 8·3%). This ether (2 g.) was shaken with a saturated solution of sodium hydrogen sulphite for 3 hours, the solid adduct decomposed with sodium carbonate, and the small amount of oil distilled; 1 : 2 : 3 : 4 : 5 : 8-*hexahydro-2-ketonaphthalene* had b. p. 85—90°/0·3 mm. (Found : C, 81·0; H, 7·8. $C_{10}H_{14}O$ requires C, 81·0; H, 8·1%). The only band in the ultra-violet above 2200 A. was a small one at $\lambda_{max.}$ 2740 (ε 200) (ethanol), probably due in part to the carbonyl group and in part to impurity. The 2 : 4-dinitrophenylhydrazone had m. p. 171°. After addition of a small crystal of toluene-*p*-sulphonic acid to the tetrahydrohydroxyethoxynaphthalene (1·1 g.) the temperature immediately rose. After 10 minutes the mixture was neutralised with gaseous ammonia and distilled, having b. p. 108—109°/0·8 mm. The substance appears to be 1 : 2 : 3 : 4 : 5 : 8-*hexahydro-2-ketonaphthalene ethylene ketal* (1 : 2 : 3 : 4 : 5 : 8 : 4′ : 5′-*octahydro*-1′ : 2′-*dioxole*-2′-spiro-2-*naphthalene*) (V) (Found : C, 74·7; H, 7·9. $C_{12}H_{18}O_{2}$ requires C, 75·0; H, 8·3%).

1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-*Octahydro-2-ketonaphthalene* (X).—1 : 2 : 3 : 4-Tetrahydro-6-methoxynaphthalene (40 g.; Stork, *J. Amer. Chem. Soc.*, 1947, **69**, 576) in ethanol (400 c.c.), ether (400 c.c.), and ammonia (2·5 l.) was reduced with sodium (40 g.). The product, worked up as usual, was dissolved in a little ether and shaken for 1·5 hours with hydrochloric acid at pH 2—3, and the resulting oil shaken with aqueous sodium hydrogen sulphite for 4 hours. The solid adduct was separated by centrifugation followed by filtration, and thoroughly washed with ether. The ethereal filtrate was concentrated and re-treated with sodium hydrogen sulphite. Four such treatments resulted in the separation of 36 g. of adduct. For some reason as yet undefined one treatment, no matter how prolonged, was insufficient. The solid was decomposed by shaking it with N-sodium carbonate solution (500 c.c.) and ether (300 c.c.), followed by further ether-extraction. 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-*Octahydro-2-ketonaphthalene* so obtained (12 g.) had b. p. 85—87°/1·25 mm. (Found : C, 79·8; H, 9·1. $C_{10}H_{14}O$ requires C, 80·0; H, 9·35%). The ultra-violet absorption showed a small band at $\lambda_{max.}$ 2810 A. (ε 37·9), $\lambda_{min.}$ 2700 A. (ε 35·5). The 2 : 4-*dinitrophenylhydrazone* was obtained as yellow needles (from ethyl acetate–ethanol), m. p. 167·5—168·5° (Found : C, 58·5; H, 5·7; N, 17·15. $C_{16}H_{18}O_{4}N_{4}$ requires C, 58·2; H, 5·45; N, 17·0%).

The residual material after the bisulphite treatment gave a fraction, b. p. 44—70°/1 mm., which did not react with Brady's reagent, and a fraction (5·1 g.), b. p. 79—83°/1 mm., which gave rise to the 2 : 4-dinitrophenylhydrazone, m. p. 169—171°, of the isomeric conjugated ketone 1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-octahydro-6-ketonaphthalene. Attempts to alkylate 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-octahydro-2-ketonaphthalene with 2-phenylethyl bromide and sodium or potassium amide in liquid ammonia, benzene, or ether, resulted surprisingly in recovery of most of the ketone.

2 : 3 : 4 : 5 : 8 : 7 : 8 : 9 : 10 : 14-*Decahydro-2-ketophenanthrene* (XI).—Diethylaminobutanone (4·315 g.) (Wilds and Shunk, *J. Amer. Chem. Soc.*, 1943, **65**, 469) was treated with methyl iodide (4·29 g.) in a 500-c.c. flask, the technique of Cornforth and Robinson (*J.*, 1949, 1855) being used. To it was added 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-octahydro-2-ketonaphthalene (4·526 g.) in benzene (20 c.c.), under a nitrogen atmosphere, followed by a solution of potassium (1·175 g.) in ethanol (20 c.c.) during 5 minutes with ice-cooling. The flask was swirled until the methiodide had disappeared, the mixture left for 1 hour, refluxed for 5 minutes, cooled, and acidified with 2N-sulphuric acid, and the product extracted with ether.

The dark red oil so obtained was dissolved in light petroleum (b. p. 60—80°) and passed through a column of activated alumina, elution being carried out with light petroleum (b. p. 60—80°). The fraction so obtained (0·82 g.) consisted essentially of unchanged octalone, and the addition of increasing amounts of ethyl acetate, up to 10%, to the eluent then gave first a mixture (0·91 g.) forming a non-crystalline derivative with Brady's reagent, followed by a viscous oil (0·8 g.) giving rise to 2 : 3 : 4 : 5 : 6 : 7 : 8 : 9 : 10 : 14-*decahydro-2-ketophenanthrene* 2 : 4-*dinitrophenylhydrazone* as cherry-red needles (from ethyl acetate–ethanol), m. p. 175° (Found : C, 62·7; H, 5·6; N, 14·6. $C_{20}H_{22}O_4N_4$ requires C, 62·8; H, 5·8; N, 14·7%). The absorption at $\lambda_{max.}$ 4000 (ε 20,000), $\lambda_{max.}$ 2595 A. (ε 16,700) (in chloroform) indicates the presence of conjugated double bonds in the ketone (cf. Braude and Jones, *loc. cit.*; Djerassi and Ryan, *J. Amer. Chem. Soc.*, 1949, **71**, 1000). The remaining material on the column was a yellow-brown fluorescent gum, not showing phenolic properties and giving an amorphous derivative with Brady's reagent.

The crude decahydroketophenanthrene (0·8 g.) was reduced with sodium (5 g.) and ethanol (50 c.c.), and then dehydrogenated with 25% palladium–charcoal (105 mg.) at 290—300° for 3 hours. The product was extracted with benzene and passed through an alumina column to remove gross impurities. The semi-solid product was then chromatographed in light petroleum (b. p. 40—60°), the first gummy eluate being followed by phenanthrene (210 mg.), m. p. 98—98·5° (picrate, m. p. 143—144°; trinitrobenzene complex, m. p. 162°); all these m. p.s were undepressed by authentic specimens.

2 : 3 : 4 : 5 : 6 : 7 : 8 : 10 : 11 : 14-*Decahydro-2-ketoanthracene* (XII).—Ethyl formate (15 c.c.) in benzene (15 c.c.) was added under nitrogen to pure dry sodium methoxide from the metal (2·154 g.) and, after 15 minutes, 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-octahydro-2-ketonaphthalene (4·4 g.) was added in benzene (25 c.c.). The deep yellow mixture was left for 1·5 hours and worked up as usual for the isolation of the formyl compound, a brownish oil, which, after being kept at 0·1 mm. for 3 hours (nitrogen), solidified to a buff-coloured solid (4·9 g.) giving an intense purple colour with alcoholic ferric chloride. It was treated with diethylaminobutanone (3·94 g.), methyl iodide (3·92 g.), and potassium (1·205 g.) in ethanol (30 c.c.) as described above, and the reaction product refluxed for 25 minutes under nitrogen after the addition of a further amount (0·41 g.) of potassium in ethanol (30 c.c.). After acidification with 2N-sulphuric acid the mixture was thoroughly extracted with ether, the ethereal solution washed with 2% sodium hydroxide solution to remove unchanged formyl compound (1·36 g.), and the ether was removed. The viscous oil was taken up in light petroleum (b. p. 40—60°) containing a few drops of ethyl acetate, whereupon a solid was precipitated as colourless needles, m. p. 178—184° after crystallisation from benzene. Good analyses were difficult to obtain, apparently because of retention of solvent, but after sublimation at 100°/6 × 10^{-4} mm. analyses were approximately correct for 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 : 9 : 10 : 13 : 14-*dodecahydro-13-hydroxy-2-ketoanthracene* (Found: C, 75·9; H, 9·2. $C_{14}H_{20}O_2$ requires C, 76·4; H, 9·0%). The m. p. range, unchanged by crystallisation, may be indicative of admixture of a stereoisomer, or of decomposition.

The viscous oil obtained by evaporation of the mother-liquor from the above crystallisation was dissolved in methanol (50 c.c.) and added to potassium hydroxide (20 g.) in methanol (450 c.c.) and water (40 c.c.) under nitrogen. After 2·5 hours the solution was poured into brine (1500 c.c.) and extracted with ether (4 × 200 c.c.). The brown oil on distillation gave a fraction (1·53 g.), b. p. 155—160°/0·1 mm., which solidified. This was taken up in light petroleum (b. p. 60—80°) and chromatographed on alumina (30 g.), with light petroleum (b. p. 60—80°) as the eluent. The first material obtained was a little non-ketonic oil, followed by crystalline material (0·600 g.). The 2 : 3 : 4 : 5 : 6 : 7 : 8 : 10 : 11 : 14-*decahydro-2-ketoanthracene* crystallised from light petroleum (b. p. 40—60°) as needles, m. p. 102—103° (Found : C, 83·4; H, 9·2. $C_{14}H_{18}O$ requires C, 83·2; H, 8·9%). The absorption (ethanol) showed a band at $\lambda_{max.}$ 2940 A. ($\varepsilon_{max.}$ 30,000) in accord with the assigned structure. Treatment with Brady's reagent in the cold gave a product capable of separation into two fractions: (A), soluble in ethyl acetate from which it separated as long cherry-red needles, m. p. 215—217° (rapid heating) (Found : C, 63·3; H, 6·0; N, 14·5. $C_{20}H_{22}O_4N_4$ requires C, 62·8; H, 5·8; N, 14·7%); and (B), only slightly soluble in ethyl acetate, crystallised from ethyl acetate–toluene as dark purple needles, m. p. 254—255° (Found : C, 63·1; H, 5·7; N, 14·8%). They are probably syn- and anti-*forms* of the 2 : 4-*dinitrophenylhydrazone* of the above ketoanthracene; (A) showed absorption at $\lambda_{max.}$ 4000 (ε 32,300), 3150 (ε 9500), and 2650 A. (ε 17,500), and (B) absorbed at $\lambda_{max.}$ 3950 (ε 26,700), and 2590 A. (ε 14,700) (in chloroform). Compound (A), kept in ethyl acetate containing a little hydrochloric acid for a day, was transformed into (B).

The dodecahydrohydroxyketoanthracene, m. p. 178—184°, on treatment with alkali as above gave rise to the decahydroketoanthracene, m. p. 102—103°, in quantitative yield. The latter (0·269 g.) was reduced with sodium (1·71 g.) and ethanol (40 c.c.) and dehydrogenated with 25% palladium–charcoal (0·262 g.) at 300° for 3·5 hours. The product obtained by extraction with benzene and passage through alumina (25 g.) was anthracene (0·06 g.), m. p. 212—214° (trinitrobenzene complex, m. p. 163—164°), both m. p.s being undepressed by authentic specimens.

Disproportionation and Oxidation of 1 : 4 : 5 : 8-*Tetrahydro-2-methoxynaphthalene.*—The methoxytetralin (10 g.) was added to freshly prepared Raney nickel (*ca.* 1 c.c.) in ethanol (40 c.c.), with stirring. The mixture became warm and was refluxed for 30 minutes, then filtered, and the ethanol removed under reduced pressure. The residual oil in ethanol gave a picrate, whence aqueous ammonia (3%) afforded 2-methoxynaphthalene (1·3 g.), m. p. 70°. Most of the alcohol was removed from the filtrate, which was poured into aqueous ammonia and extracted with ether (100 c.c.). Removal of the solvent and distillation gave an oil, b. p. 122—126°/14 mm., which after being boiled with 3% sulphuric acid (10 minutes) gave a small amount of a crystalline bisulphite compound, decomposed by sodium carbonate to 1 : 2 : 3 : 4-tetrahydro-2-ketonaphthalene (0·3 g.). The material recovered after the bisulphite treatment was added to a solution of potassium amide (from the metal, 5 g.) in liquid ammonia (100 c.c.) with development of a deep red colour. Distillation of the product gave two fractions: (A) b. p. 90—

96°/14 mm., and (B) b. p. 135—138°/16 mm. Redistillation of (A) over sodium gave a colourless oil (2·0 g.), b. p. 208° (odour of tetralin), which is probably a mixture of dihydronaphthalenes (Found: C, 92·1; H, 7·9. Calc. for $C_{10}H_{10}$: C, 93·3; H, 7·7%). This corresponds to 1 : 2 : 3 : 4-tetrahydro-2-methoxynaphthalene (2·5 g.) in the original disproportionation product. Fraction (B) (3·5 g.) was oxidised with chromic acid (Stork, *loc. cit.*) to 1 : 2 : 3 : 4-tetrahydro-1-keto-6-methoxynaphthalene, m. p. 79°, and is therefore 1 : 2 : 3 : 4-tetrahydro-6-methoxynaphthalene.

To a stirred solution of 1 : 4 : 5 : 8-tetrahydro-2-methoxynaphthalene (2·97 g.) in dry benzene (20 c.c.) was slowly added lead tetra-acetate (8·1 g.) with cooling in water. After 15 minutes the lead acetate was removed by filtration and the product distilled (2·04 g.; b. p. 86—100°/1 mm.). It was heated with 2N-sulphuric acid (20 c.c.) under nitrogen for 15 minutes, taken up in ether, and shaken with saturated aqueous sodium hydrogen sulphite for 3 hours. A small amount of the bisulphite derivative of 1 : 2 : 3 : 4-tetrahydro-2-ketonaphthalene was removed by filtration, and gave after decomposition with sodium carbonate the ketone (*ca.* 60 mg.). The residual oil was dissolved in light petroleum (b. p. 40—60°) and cooled in carbon dioxide–acetone, to yield 2-methoxynaphthalene (0·4 g.), m. p. 70°. The action of bromine in carbon tetrachloride on the light petroleum solution gave 2 : 3-dibromo-1 : 4-dihydro-6-methoxynaphthalene, m. p. 97° (cf. Beer, *loc. cit.*) (Found: C, 41·3; H, 3·9. Calc. for $C_{11}H_{12}OBr_2$: C, 41·2; H, 3·75%).

1 : 4-*Dihydro*-5-2′-*hydroxyethoxynaphthalene* (XV).—1-2′-Hydroxyethoxynaphthalene (30 g.; b. p. 194—196°/15 mm.) in methanol (36 c.c.) and ammonia (200 c.c.) was reduced with sodium (13 g.). Distillation of the product gave a viscous oil (26 g.), b. p. 138—142°/0·3 mm., which solidified to give 1 : 4-*dihydro*-5-2′-*hydroxyethoxynaphthalene*, long needles (from light petroleum, b. p. 40—60°), m. p. 56° (Found: C, 75·8; H, 7·6. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%). In an endeavour to produce more profound reduction the hydroxyethoxynaphthalene (10 g.) was treated in methanol (31 c.c.) and ammonia (200 c.c.) with sodium (12 g.). Worked up in the usual way, the product gave the following fractions: (A), b. p. 80—85°/20 mm. (1·5 g.); (B), b. p. 152—160°/18 mm. (4·6 g.); and (C), b. p. 160—184°/18 mm. (2·6 g.). Fraction (A) partly solidified to give 1 : 4 : 5 : 8-tetrahydronaphthalene, m. p. 42°, and from (C) was obtained crystalline 1 : 4-dihydro-5-2′-hydroxyethoxynaphthalene (1·2 g.), m. p. 56°. Fraction (B) with cold Brady's reagent gave mixed 2 : 4-dinitrophenylhydrazones, m. p. 175—200°, which were fractionally crystallised from benzene–light petroleum (b. p. 40—60°) to give what appear to be three distinct *compounds*: (D), bright red needles, m. p. 238° (Found: C, 58·6; H, 5·3; N, 17·55. $C_{16}H_{16}O_4N_4$ requires C, 58·6; H, 4·9; N, 17·1%); (E), orange plates, m. p. 152—155° (Found: C, 59·0; H, 5·4; N, 17·2%); and (F), orange-yellow plates, m. p. 144° (Found: C, 58·1; H, 5·2; N, 17·2%). Both (E) and (F) were converted into (D) by hot alcoholic sulphuric acid, and the three compounds are probably bond-isomers. Attempts to isolate a uniform ketone after acid hydrolysis of (B) were unsuccessful. Heating with sulphuric acid (10%) under reflux in nitrogen for 10 minutes afforded a mixture, b. p. 110—145°/10 mm., giving a mixed derivative, m. p. 180—200°, with 2 : 4-dinitrophenylhydrazine; after the fraction (B) had been shaken in ethyl acetate solution for 30 minutes with aqueous sulphuric acid at pH 4 a *product*, possibly mainly a cyclic acetal, was isolated, having b. p. 132°/16 mm. (Found: C, 74·3; H, 8·7. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·3%); it showed an ill-defined inflection at 2240—2330 A.

Reduction of 1 : 2 : 3 : 4-*Tetrahydro*-5-2′-*hydroxyethoxynaphthalene*.—1 : 2 : 3 : 4-*Tetrahydro*-5-2′-*hydroxyethoxynaphthalene* was made in the standard manner from 1 : 2 : 3 : 4-tetrahydro-5-hydroxynaphthalene by the action of an excess of ethylene chlorohydrin and aqueous alkali. It had b. p. 143°/0·25 mm., m. p. 52° [from light petroleum (b. p. 40—60°)] (Found: C, 75·0; H, 8·3. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·3%). The ether (15 g.) in ethanol (25 c.c.) was added to ammonia (250 c.c.) and reduced with sodium (10 g.). Distillation of the product gave (A) (*ca.* 1 g.), b. p. 90°/10 mm., and (B) (11·5 g.), b. p. 135—140°/0·2 mm. Fraction (A) after re-distillation over sodium had b. p. 203—204°, n_D^{15} 1·5162, and appeared to be a hydrocarbon mixture. Fraction (B) was refluxed with 0·5N-sulphuric acid for an hour, and the product taken up in ether and distilled (b. p. 120—140°; 5 g.). A small residue from the distillation crystallised and proved to be unchanged starting material. Redistillation gave two fractions: (C), (0·9 g.) b. p. 120—123°/13 mm., and (D), b. p. 134—136°/13 mm. (3·9 g.). Fraction (C) on treatment with sodium hydrogen sulphite solution gave a small amount of the derivative of decahydro-1-ketonaphthalene; fraction (D) was 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-octahydro-1-ketonaphthalene (Found: C, 80·4; H, 9·4. Calc. for $C_{10}H_{14}O$: C, 80·0; H, 9·4%). The 2 : 4-dinitrophenylhydrazone had m. p. 262° (Found: N, 16·5. Calc. for $C_{16}H_{18}O_4N_4$: N, 16·9%); its m. p. was undepressed by an authentic specimen.

Reduction 5 : 6 : 7 : 8-*Tetrahydro*-3-*methoxy*-2-*naphthoic acid*.—The dry sodium salt of 1 : 2 : 3 : 4-tetrahydro-6-hydroxynaphthalene was heated to 190° for 2 hours in an atmosphere of carbon dioxide. The acid portion of the product was methylated by the repeated action of methyl sulphate and sodium hydroxide until a test portion on acidification produced a crystalline acid not giving a purple colour with ferric chloride. The 5 : 6 : 7 : 8-*tetrahydro*-3-*methoxy*-2-*naphthoic acid*, precipitated on acidification of the solution, crystallised from aqueous acetic acid as long prisms, m. p. 115° (Found: C, 70·0; H, 6·8. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%). To form its sodium salt the acid (5 g.) was added to the product from sodium (0·6 g.) and ethanol (30 c.c.) in ammonia (300 c.c.), and reduction was carried out by addition of sodium (6 g.) in small pieces. After addition of water (150 c.c.) most of the ammonia was removed under reduced pressure; ether-extraction of the solution gave no product. Acidification to Congo-red paper gave an oil and, on boiling, carbon dioxide was evolved. The oil was taken up in ether and separated into fractions soluble and insoluble in aqueous sodium carbonate. The neutral fraction (0·8 g.) had b. p. 120—135°/11 mm. On treatment with aqueous sodium hydrogen sulphite it gave a crystalline solid (A) and unchanged oil (B). The adduct (A) was decomposed by shaking it with dilute hydrochloric acid and ether for an hour. The resulting small amount of pleasant-smelling oil gave 1 : 2 : 3 : 4 : 5 : 6 : 7 : 10-*octahydro*-6-*ketonaphthalene* 2 : 4-*dinitrophenylhydrazone*, m. p. 134—135° (Found: C, 57·7; H, 5·3. $C_{16}H_{18}O_4N_4$ requires C, 58·2; H, 5·4%). The formulation is based on the

orange-yellow colour of the derivative, and the fact that by alcoholic sulphuric acid it was converted into the derivative, m. p. 188—189°, of (B). Fraction (B), b. p. 125—128°/14 mm., gave 1 : 2 : 3 : 4 : 5 : 6 : 9 : 10-*octahydro*-6-*ketonaphthalene* 2 : 4-*dinitrophenylhydrazone* as dark red prisms, m. p. 188—189° (Found: C, 58·3; H, 5·4%).

Reduction of 5 : 6 : 7 : 8-*Tetrahydro*-1-*methoxy*-2-*naphthoic acid.*—The acid was prepared as above, starting from 1 : 2 : 3 : 4-tetrahydro-5-naphthol; methylation of the hydroxy-acid required a very large excess of methyl sulphate. 5 : 6 : 7 : 8-*Tetrahydro*-1-*methoxy*-2-*naphthoic acid* formed prisms (from aqueous acetic acid), m. p. 116—117° (Found: C 70·1; H, 6·8. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%). Reduced as above, the acid (10 g.) gave a neutral fraction (0·7 g.), b. p. 115—125°/14 mm. This partly crystallised in the refrigerator, and crystallised from light petroleum (b. p. 40—60°) as prisms, m. p. 72—73°, which appear to be 1 : 2 : 3 : 4 : 5 : 8 : 9 : 10-*octahydro*-5-*ketonaphthalene* (Found: C, 79·5; 9·1. $C_{10}H_{14}O$ requires C, 80·0; H, 9·35%). The 2 : 4-*dinitrophenylhydrazone* formed bright red prisms (from ethyl acetate), m. p. 207° (Found: C, 57·8; H, 5·3. $C_{16}H_{18}O_4N_4$ requires C, 58·2; H, 5·4%). The acid fraction from the reduction was a thick oil (7·6 g.) which was oxidised in acetic acid (20 c.c.) by chromium trioxide (3 g.) in water. After the exothermic reaction was complete, addition of water gave a white solid which crystallised from aqueous acetic acid as long needles, m. p. 142° undepressed by an authentic specimen of 1 : 2 : 3 : 4-tetrahydro-6-naphthoic acid.

Ultra-violet and infra-red absorption spectra are by Dr. F. B. Strauss (Oxford) and Dr. R. N. Haszeldine (Cambridge).

This work was carried out during the tenure of the Smithson Research Fellowship of the Royal Society (A. J. B.) and of a maintenance Grant from the D.S.I.R. (H. S.). The authors are indebted to the Nuffield Research Foundation for financial assistance.

THE UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, April 4th*, 1951.]

---

437. *Theoretical Investigation of Reactivities of Conjugated Bonds. Part II.* The Significance of Some Theoretical Quantities.*

By R. D. BROWN.

The significance of the various theoretical quantities which have been suggested as criteria of bond reactivity is studied in detail. It is shown that the bond-localization energy represents an attempt, subject to some approximations, to compute the heat of activation of a bond reaction. Other theoretical quantities such as mobile-bond order and free valence are shown to be related to the first terms of Taylor series for the bond-localization energy. Their successful correlation with experimental reactivities depends upon empirical relations of a statistical nature existing between bond-localization energy and successive terms of its Taylor expansion.

Some additional advantages of discussing bond reactivities in terms of bond-localization energies are indicated.

IN Part I * it was shown that the localization theory provides a very satisfactory interpretation of the relative reactivities of conjugated bonds towards reagents such as osmium tetroxide. A series of notes has recently appeared discussing the relative reactivities of the three dinaphthylethylenes in terms of various theoretical quantities (Badger, *Nature*, 1950, **165**, 647; Coulson, *J.*, 1950, 2252; Daudel, *Compt. rend.*, 1950, **231**, 908; Berthier, Berthod, Mayot, and Pullman, *ibid.*, p. 1149) and it would seem desirable to assess the relative merits of these quantities as criteria of reactivity.

The thermodynamic treatment of reaction rates (Wynne-Jones and Eyring, *J. Chem. Physics*, 1935, **3**, 492; Glasstone, Laidler, and Eyring, "The Theory of Rate Processes," 1941, p. 195) leads to the equation

$$k = \frac{kT}{h} \cdot \exp(\Delta S^{\ddagger}/R) \cdot \exp(-\Delta H^{\ddagger}/RT) \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

and ideally we should discuss the relative rate constants in terms of the entropy of activation, $\Delta S^{\ddagger}$, and the heat of activation, $\Delta H^{\ddagger}$. Molecules which react readily with osmium tetroxide are for the most part of such complexity that it is not feasible to calculate $\Delta S^{\ddagger}$ by means of the appropriate partition functions, so the assumption has to be made that the entropies of activation are the same for the reactions of two different bonds, either in the same or in different

* Part I, *J.*, 1950, 3249.

molecules, with osmium tetroxide. This of course requires $RT \log (k_a/k_b)$ to be independent of temperature, where k_a and k_b are the rate constants for reaction of the two bonds considered at the same temperature. Although rates of reaction of a number of hydrocarbons have been measured (Badger, *J.*, 1949, 456; 1950, 1809; Badger and Lynn, *J.*, 1950, 1726) their temperature dependence has not, so this assumption has not been tested directly so far. However, the approximate quantitative success of the localization theory (Part I) suggests that the assumption is reasonable.

The discussion of relative rates is thus reduced to a discussion of the relative values of $\Delta H^{\ddagger}$. Dewar (*Trans. Faraday Soc.*, 1946, **42**, 767) has in effect shown that the simple molecular-orbital approximation, using an appropriate value for the parameter γ, provides a reliable estimate of the contribution to the molecular *heat content* due to the π-electrons. The environments of reactive bonds in polycyclic hydrocarbons are so similar that differences in heats of activation for such bonds will in good approximation be due to differences in the contributions made by the π-electrons. Again this is borne out indirectly by the approximate quantitative success of the localization theory. The formation of the activated complex will be accompanied by a partial localization of the π-electrons, so the contribution of the latter to the heat of activation may be termed the *heat of localization*. This quantity will provide a relatively sound basis for discussion of relative reactivities of conjugated bonds.

The various theoretical quantities which have been correlated with bond reactivities are, of course, concerned only with the π-electrons, so it is to be expected that the relative merits of these quantities are determined by their degree of correlation with the heat of localization, $\Delta H_{\pi}^{\ddagger}$. The ultimate requirement for reaction of a bond with a molecule of osmium tetroxide is that the former must supply two π-electrons to bind the osmium tetroxide to the carbon atoms at each end of the bond. The π-electron heat of reaction, ΔH_{π}, will consequently be the difference in π-electron heat content of the conjugated system left after reaction (the residual molecule) and of the original conjugated system (apart from some constant amount arising from the π-electrons which form the σ-bonds with the OsO_4 molecule).

The bond-localization energy, B, represents the molecular orbital approximation to ΔH_{π} and the use of this as a criterion of bond reactivity supposes that $\Delta H_{\pi}^{\ddagger}$ is proportional to ΔH_{π}. The rough quantitative success of the localization theory suggests that if an appropriate value of γ is employed, B is in fact a good approximation to $\Delta H_{\pi}^{\ddagger}$. We conclude then that the bond-localization energy is a very good criterion of bond reactivity.

Next we may consider the mechanism of the formation of the activated complex. If it is supposed that the approach of the osmium tetroxide to a particular bond occasions an alteration in the magnitude of the coulomb integrals of the atoms at either end of the bond under consideration, then the change in π-electron heat content may be expanded as a Taylor series:

$$\delta H_{\pi} = (\partial H_{\pi}/\partial \alpha_a)\delta\alpha_a + (\partial H_{\pi}/\partial \alpha_b)\delta\alpha_b + \tfrac{1}{2}\{(\partial^2 H_{\pi}/\partial \alpha_a^2)(\delta\alpha_a)^2 + 2(\partial^2 H_{\pi}/\partial\alpha_a\partial\alpha_b)\delta\alpha_a\delta\alpha_b + (\partial^2 H_{\pi}/\partial\alpha_b^2)(\delta\alpha_b)^2\} + \quad . \quad . \quad . \quad . \quad . \quad (2)$$

α_a, α_b, being the coulomb integrals of atoms a and b at either end of the bond (I). If it is supposed that both coulomb integrals are perturbed by the same amount, *i.e.*

(I.)

$$\delta\alpha_a = \delta\alpha_b = X\beta \text{ (say)},$$

where β is the resonance integral of a benzene bond, and the differential coefficients in equation (2) are identified with the electron densities, q, and the mutual polarizabilities, π (Coulson and Longuet-Higgins, *Proc. Roy. Soc.*, *A*, 1947, **191**, 39), then equation (2) becomes:

$$\delta H_{\pi} = (q_a + q_b)X\beta + \tfrac{1}{2}(\pi_{a,a} + 2\pi_{a,b} + \pi_{b,b})X^2\beta^2 + \quad . \quad . \quad . \quad . \quad (3)$$

Now the polarizabilities are computed in units of $1/\beta$, so it is convenient to write:

$$S = \beta(\pi_{a,a} + 2\pi_{a,b} + \pi_{b,b}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

and furthermore all hydrocarbons so far studied experimentally are alternant hydrocarbons, for which $q_a = q_b = 1$, so we finally have:

$$\delta H_{\pi} = (2X + \tfrac{1}{2}SX^2 + \ldots.)\beta \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

It seems reasonable to assume that the magnitude of the perturbation, X, is determined only by the nature of the attacking molecule and its distance from the bond undergoing addition. Then, since the C–O bond lengths in activated complexes of the most reactive bonds of polycyclic hydrocarbons must surely be very similar, the relative changes in H_{π} for the different bonds considered will be determined by the relative values of the sum of polarizabilities, S, *provided*

that the higher terms in the expansion (5) *can be neglected.* The latter will be the case if X is sufficiently small, but unfortunately there is at present no way of determining the value of X appropriate to the activated complex, and even its sign is not certain because bond reagents are neither electrophilic nor nucleophilic. We cannot therefore decide whether the values of S for various bonds will give a qualitative indication of H_π except by comparison with, say, the corresponding bond-localization energies. We have given some values for the two quantities in Table I.

TABLE I.*

Hydrocarbon.	Bond.	S.	$B(-\beta)$.	Hydrocarbon.	Bond.	S.	$B(-\beta)$.
Benzene	—	0·481	1·528	Ethylene	—	0	0
Naphthalene	1 : 2	0·422	1·259	Butadiene	1 : 2	0·224	0·472
	2 : 3	0·590	1·729		2 : 3	0·714	2·472
Anthracene	1 : 2	0·404	1·204	Hexatriene	1 : 2	0·322	0·516
	2 : 3	0·590	1·786		2 : 3	0·791	2·298
					3 : 4	0·332	0·988
Phenanthrene	1 : 2	0·455	1·319				
	2 : 3	0·563	1·655				
	3 : 4	0·458	1·338				
	9 : 10	0·345	1·065				

* Polarizability data taken from Coulson and Longuet-Higgins, *Proc. Roy. Soc.*, *A*, 1947, **192**, 16; *J.*, 1949, 971.

The correlation of S with B is reasonably good (for the cyclic hydrocarbons the points all lie close to a straight line passing through the origin), but unfortunately in the wrong sense. As S is a positive number, and β a negative energy quantity, the smallest activation energy would correspond to the *greatest* value of S, and to the *smallest* value of B. It will be noticed that the reactive bonds correspond to the smallest values of S however. We are forced to the conclusion that the higher terms in the expansion (5) are important or that *the attacking molecule gives rise to other more important perturbations.*

The next possibility is that the osmium tetroxide produces a change in the resonance integral, β_{ab}, between the atoms a and b. Proceeding in the same way we write

$$\delta H_\pi = (\mathrm{d}H_\pi/\mathrm{d}\beta_{ab})\delta\beta_{ab} + (\mathrm{d}^2H_\pi/\mathrm{d}\beta_{ab}^2)(\delta\beta_{ab})^2/2\,! + \ldots \quad (6)$$

$$= 2p_{ab}\delta\beta_{ab} + \tfrac{1}{2}\pi_{ab,\,ab}(\delta\beta_{ab})^2 + \ldots \quad (7)$$

and, if it is assumed that $\delta\beta_{ab}$ has the same value for all activated complexes, the relative values of δH_π will be determined by the mobile bond orders, p_{ab}, of the various bonds considered, provided that the second and higher terms are negligible. Again this will depend upon the

TABLE II.

Hydrocarbon.	$B(-\beta)$.	p.	T.	ΣF.
Pentaphene	1·006	0·790	1·936	0·812
1 : 2-Benzanthracene	1·030	0·783	1·974	0·807
1 : 2-7 : 8-Dibenzanthracene	1·041	0·780	1·992	0·804
1 : 2-5 : 6-Dibenzanthracene	1·045	0·778	2·000	0·804
Pyrene	1·057	0·777	2·012	0·800
Phenanthrene	1·065	0·775	2·024	0·798
3 : 4-Benzophenanthrene	1·102	0·762	2·082	0·795
Picene	1·108	0·758	2·098	0·795
Chrysene	1·121	0·754	2·118	0·793
Pentacene	1·183	0·742	2·216	0·768
Naphthacene	1·188	0·741	2·222	0·767
Anthracene	1·204	0·738	2·242	0·763
1 : 2-3 : 4-Dibenzanthracene	1·241	0·727	2·292	0·760
Naphthalene	1·259	0·725	2·316	0·752
Triphenylene	1·383	0·690	2·480	0·740
Benzene	1·528	0·667	2·667	0·693

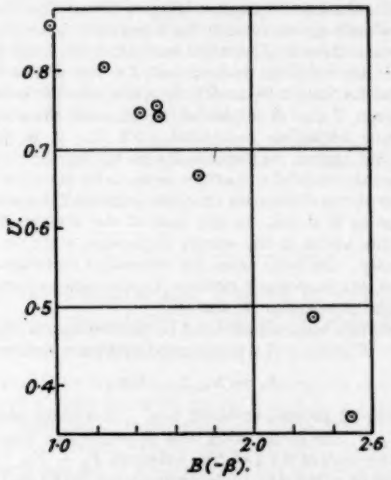
magnitude of $\delta\beta_{ab}$. It would be expected that $\delta\beta$ is negative,† so that if p_{ab}, the mobile order of bond ab, does determine the π-electron heat of activation, then the most reactive bond would be that of highest mobile order. The fact that mobile-bond order has been widely used as an index of bond reactivity (*e.g.*, Badger, *J.*, 1950, 1809), together with the very high degree of

† This supposes that the mechanism of addition consists first in increasing the mobile order of the bond ab to a value approaching that of ethylene, followed by addition to this perturbed bond. One could, however, imagine mechanisms which would require $\delta\beta$ to be positive. The correlation of these p_{ab} values with B_{ab} indicates that these latter mechanisms must be rejected.

correlation of p with bond-localization energy of the most reactive bond for a considerable number of polycyclic hydrocarbons (Table II), suggests that $\delta\beta$ is relatively small. Some idea of the changes involved can be gained as follows. It has been found empirically (Brown, unpublished work) that

$$dp_{ab}/d\beta_{ab} = \pi_{ab,\,ab} \simeq 3(1 - p_{ab})/4\beta \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

for various bonds in isolated molecules. If we suppose that this approximation also holds for a small change in the resonance integral of a given bond, then we may integrate expression (8) to derive δp_{ab} from $\delta\beta_{ab}$. Suppose that p_{ab} is increased from 0·8 to 0·9; a simple calculation shows that this corresponds to $\delta\beta_{ab} = \beta\frac{4}{3}\log 2 \simeq 0{\cdot}9\beta$. Such an estimate of $\delta\beta$ cannot be regarded as quantitatively reliable but it serves to show that the value of $\delta\beta$ corresponding to formation of the activated complex is not likely to be so small that the second and higher terms in equation (7) can be neglected (for bonds of mobile order around 0·7 to 0·8, $\pi_{ab,\,ab}/2$ is of the order of $0{\cdot}1/\beta$).



It would seem that the success of the correlation of, say, p_{ab} with B_{ab} is due in part to the additional linear relation (8) between $\pi_{ab,\,ab}$ and p_{ab}, and hence between $\pi_{ab,\,ab}$ and B_{ab}. It is quite possible that higher terms are similarly related to B, but they have not so far been investigated.

It is of interest to put $\delta\beta_{ab} = X\beta$ in expression (7) and to substitute (8) for $\pi_{ab,\,ab}$. The result is

$$\delta H_\pi = [3X + (16 - 3X)p + \ldots]X\beta/8 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

so that, provided that the effect of higher terms can be neglected, one would obtain an inverse correlation of p with δH_π unless X is smaller than 16/3; such a huge perturbation to β_{ab} would not be physically reasonable, but equation (9) brings out the opposing tendencies of p and π on δH_π.

Neither of the localization mechanisms so far considered corresponds to localization of the bond under consideration; their effect is to build up the electron density in the bond or at the atoms at either end of it. Localization of the bond is achieved, however, if the resonance integrals of all adjoining bonds are reduced in magnitude. Again the heat content change may be expanded as

$$\begin{aligned}\delta H_\pi &= (\partial H_\pi/\partial\beta_{ca})\delta\beta_{ca} + (\partial H_\pi/\partial\beta_{bd})\delta\beta_{bd} \\ &\quad + [(\partial^2 H_\pi/\partial\beta_{ca}^2)(\delta\beta_{ca})^2 + 2(\partial^2 H_\pi/\partial\beta_{ca}\partial\beta_{bd})\delta\beta_{ca}\delta\beta_{bd} \\ &\quad\quad + (\partial^2 H_\pi/\partial\beta_{bd}^2)(\delta\beta_{bd})^2]/2 + \ldots\ldots \\ &= 2(p_{ca} + p_{bd})X\beta + (\pi_{ca,\,ca} + 2\pi_{ca,\,bd} + \pi_{bd,\,bd})X^2\beta^2 + \quad . \quad . \quad . \quad (10)\end{aligned}$$

assuming the resonance integral perturbations to bonds ca and bd (I) to be both equal to $X\beta$. For complete localization the corresponding value of X is of course -1, so in this case we can be fairly sure that higher terms become rapidly less important when we use the value of X corresponding to the activated complex. We can write equation (10) as

$$\delta H_r = (TX + UX^3 + \ldots\ldots)\beta \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

The values of the coefficient T are listed in Table II. These show at least as good a correlation with B as does p, and indeed it would be better to use the sum of the mobile orders of bonds adjoining a given bond as a criterion of its reactivity than to use its own mobile order. Clearly, as X is now negative, if the reactivity is determined by T, then the *smaller* T the more reactive the bond. The justification for using T in this way will depend upon the magnitude of the sum of polarizabilities, as well as of X, and so far we have established only that the latter is less than unity. Some values of U for bonds in butadiene, hexatriene, benzene, naphthalene, and styrene whose environments are similar to (I) in that they all have just two neighbouring bonds, are shown plotted against B in the accompanying figure. The values of U were computed from the polarizability data of Coulson and Longuet-Higgins (*Proc. Roy. Soc.*, *A*, 1948, **193**, 447). It is seen that the two are related approximately by a smooth curve which is nearly linear. This does not hold, however, when there is other than one adjoining bond at either end of the one in question; for example, U for ethylene is zero and for the $\alpha\beta$-bond of styrene is 0·338, and discrepancies are also found for the 9 : 10- and 1 : 9-bonds of naphthalene.

This relationship between U and B might be the cause of the correlation between T and B because U is by no means negligible compared with T. It is quite possible that similar relationships between B and higher coefficients are to be found; indeed correlations between apparently unrelated molecular-orbital quantities seem to be the rule rather than the exception.

It would seem from the above discussion that the value of T for a bond is a sounder criterion of reactivity than p, because it is only in the case of the former that we can determine the relative importance of higher terms in the energy expansion, since we know that the magnitude of X must be less than unity. In both cases the successful correlation with reactivity must in part be due to the approximate monotonic relationships mentioned above between both p and T and their higher terms in the expansions (7) and (11).

Another quantity which has been widely used in the discussion of chemical reactivity is free valence. The free valence of atom a of a conjugated system is defined by :

$$F_a = N_{max.} - \Sigma_i p_{ai} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

where the summation is over all atoms i adjacent to a. It is easily seen that $F_a + F_b$ is a linear combination of p_{ab} and T_{ab}. The latter both bear approximate linear relationships to B_{ab}, so the same must be true of the sum of the two free valences, $F_a + F_b$. Values of ΣF for the most reactive bonds of a number of polycyclic hydrocarbons are listed in Table II. The correlation with B is as good as those involving p and T, so ΣF is another quantity which could be used as a criterion of bond reactivity. It is to be emphasised, however, that the use of ΣF in this connection is as empirical as the use of p or T. The bond localization energy, B, is more fundamentally related to the heat of activation, and hence to the chemical reactivity, of a bond than is p, T, or ΣF. Nevertheless this state of affairs would be resolved if the mathematical structure of the molecular-orbital theory could be shown to imply the various statistical relations which have been found between the various theoretically defined quantities.

It has also been proposed (Badger, *J.*, 1950, 1809) to use the oxidation–reduction potential of the *o*-quinone as an index of the reactivity of a bond. The assumption here is that the transition state has a quinonoid electronic structure. However, there is no evidence on which to base this hypothesis. The correlation which Badger notes between oxidation–reduction potential and mobile-bond order is a necessary consequence of the empirical relation between p and B. The correlation with oxidation–reduction potential follows because B represents the increase in H_r in going from the original hydrocarbon to the *o*-quinone, assuming that the C=O bonds in the latter do not form a part of the conjugated system and also that the carbonyl groups do not cause any perturbations to coulomb or resonance integrals. Oxidation–reduction potentials have been discussed in terms of quantities equivalent to B (Evans, *Trans. Faraday Soc.*, 1946, **42**, 113; Diatkina and Syrkin, *Acta Physicochim.*, 1946, **21**, 921) and linear relations found between the two.

Evidently the oxidation–reduction potential is to be regarded as an empirical criterion of bond reactivity with rather less justification than p, T, and ΣF.

Finally it is to be noted that the bond-localization energy involves only energy quantities,

and that improved values of B could be obtained by refining the energy calculations. The same is not true of p, T, ΣF, and the oxidation–reduction potential. The first three are not observables, they are mathematical conveniences of the molecular-orbital theory, and there is no way of improving their calculation if the values at present used are found unsatisfactory. The other advantage of the bond-localization energy is that it is a linear function of the heat of activation and so can be employed to estimate relative reaction rate constants. This feature is particularly useful when comparing the reactivities of a pair of hydrocarbons such as 1 : 2-benzanthracene and 1 : 2-7 : 8-dibenzanthracene. The former has one bond very much more reactive than all the others while the latter, from its symmetry, has two equivalent bonds of high reactivity. The values of B, p, T, and ΣF (Table II) all indicate that the benzanthracene bond is more reactive than the dibenzanthracene bond, but the question arises whether the presence of two such bonds in dibenzanthracene will be sufficient to increase the total reactivity to more than the benzanthracene value. If we employ the values of B, then by converting them into relative rate constants and summing over all bonds in the two molecules we obtain the total reactivities of the two hydrocarbons. It is then found (Part I, Table II) that in fact the total reactivity of dibenzanthracene is greater than of benzanthracene although the most reactive bond of the latter is more reactive than the most reactive bond of the former. Clearly such a result could not have been obtained from considerations of values of p, T, or ΣF because it is not clear how the individual values are to be combined to obtain the total molecular reactivity. However, the various empirical relations with B offer a possible method of doing this when the bond localization energies have not been directly computed.

The above work was carried out during tenure of an Australian National University Travelling Scholarship. The author is grateful for the opportunity of discussing the manuscript with Professor C. A. Coulson, F.R.S.

THEORETICAL PHYSICS DEPT., KING'S COLLEGE,
STRAND, LONDON.

[*Received, February 12th*, 1951.]

---

438. *Studies of the Localization Theory of Organic Reactions. Part I. The Effects of Annelation and of Introducing Hetero-atoms.*

By R. D. BROWN.

Fundamental equations are derived for the change in localization energy of a given position in a given molecule owing to fusion of a benzene or other ring system to the molecule, or to replacement of one of the carbon atoms of the molecule by a hetero-atom. These equations apply alike to atom, bond, and para-localization energies. They are illustrated for some special cases. Some general predictions of reactivities of heterocyclic systems are made, and the need for fundamental experimentation to determine parameters for hetero-atoms is indicated.

THE localization theory of organic reactions represents an attempt to approximate to relative heats of activation for the reaction of various organic compounds with a particular reagent, such as nitronium ion, osmium tetroxide, or maleic anhydride. Its name is derived from the fact that in this approximation the formation of the activated complex is regarded as being accompanied by a partial localization of some or all of the π-electrons present in the organic molecule. The problem of substitution in substituted benzenes has been considered by Wheland (*J. Amer. Chem. Soc.*, 1942, **64**, 900), Dewar (*J.*, 1949, 463), and Longuet-Higgins (*J. Chem. Physics*, 1950, **18**, 283), in the Diels–Alder reaction by Brown (*J.*, 1950, 691, 2730), and in reaction of hydrocarbons with osmium tetroxide by Brown (*ibid.*, p. 3249). However, the general problem of the change in reactivity of a given conjugated system when a hetero-atom is introduced, when a benzene or other ring system is annelated to it, or when one or more substituents are attached to it, has not yet been considered. It is proposed to consider this problem in the present paper. The results apply quite generally to all reactions which lend themselves to treatment by the localization approximation, also both to polycyclic conjugated systems and to polyenes and aryl-polyenes, but the latter are not so suceptible to theoretical treatment owing to uncertainty in their precise stereochemistry, which is not present in the case of the relatively rigid polycyclic systems.

Annelation.—A problem of interest, particularly in the case of polycyclic hydrocarbons, is to predict the change in reactivity of a hydrocarbon when a benzene or other cyclic system is fused

to one of its bonds, *e.g.*, to predict the difference in rates of reaction of chrysene and benzochrysene with osmium tetroxide. Let the original molecule Y, have a π-electron energy $\mathbf{E}_0$, and the energy of the same molecule but with the π-electrons localized in accordance with the structure of the appropriate activated complex, be $\mathbf{E}'_0$. The localization energy for reaction of Y with some particular reagent (corresponding to the activated complex chosen) is then

$$\mathbf{L}_0 = \mathbf{E}'_0 - \mathbf{E}_0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Now suppose Y is altered by fusing to its $a:b$-bond some other ring system, X, through its $i:j$-bond. The π-electron energy of the resultant molecule is

$$\mathbf{E} = \mathbf{E}_0 + \mathbf{K}_{ab} + \mathbf{Q} . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $\mathbf{Q}$ is the π-electron energy of X minus the energy of two ethylenic π-electrons, and $\mathbf{K}_{ab}$ is termed the annelation energy of bond $a:b$ of Y; $\mathbf{K}_{ab}$ will depend upon which bond, $i:j$, of X is involved in the fusion.

It is convenient to regard (2) as defining $\mathbf{K}_{ab}$. Since $\mathbf{Q}$ depends only upon the nature of X, we have

$$\mathbf{E}' = \mathbf{E}'_0 + \mathbf{K}'_{ab} + \mathbf{Q} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

and we may combine (1), (2), and (3) to obtain

$$\mathbf{L} = \mathbf{E}' - \mathbf{E} = \mathbf{L}_0 + \mathbf{K}'_{ab} - \mathbf{K}_{ab} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Thus far (4) is an identity arising from our definitions of $\mathbf{L}$ and $\mathbf{K}$, and does not depend upon the assumption of any particular quantum-mechanical approximation for computing the π-electron energies involved. For this reason bold-face symbols have been employed. The importance of (4) lies in the fact that if we now suppose all energy quantities to be computed by the L.C.A.O. molecular orbital approximation, then L represents a good approximation to the variable portion of the activation energy of the corresponding organic reaction. Furthermore K can then be calculated from a very simple linear relationship involving only the mobile bond orders, p_{ab}, p^x_{ij}, of the bonds undergoing annelation (Brown, *Trans. Faraday Soc.*, 1950, **46**, 1013). To indicate that we now refer to molecular-orbital approximations to the various energy quantities, we shall use plain-type symbols. The precise forms of the annelation energy relationships are

$$K_{ab} = (2{\cdot}153\sqrt{p_{ab}p^x_{ij}} - 1{\cdot}733)\beta \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

$$K'_{ab} = (2{\cdot}153\sqrt{p'_{ab}p^x_{ij}} - 1{\cdot}733)\beta \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

and upon writing $p_{ab} = p^x_{ij}(1 + \delta_{ab})$, $p'_{ab} = p^x_{ij}(1 + \delta'_{ab})$, and substituting in (4) we find

$$L - L_0 = -1{\cdot}077\beta(p_{ab} - p'_{ab})\{1 - (\delta_{ab} + \delta'_{ab})/4\} \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

where the surds have been expanded by the binomial theorem. These expansions have been taken only as far as δ^2 since the annelation-energy relations (5) and (6) begin to break down when $|\delta| > 0{\cdot}1$.

The utility of (7) will be clearer from the following example. Let L represent the bond localization energy and let us take phenanthrene as the hydrocarbon Y. The only reactive bond in phenanthrene is the 9 : 10-bond, and we may consider the change in its reactivity due to fusing a benzene ring (X) to the 2 : 3-bond of phenanthrene, thus producing 1 : 2-benzanthracene. The residual molecule for addition to the 9 : 10-bond of phenanthrene is diphenyl, so for this particular case the values of the quantities appearing in (7) are

p^x_{ij} : a benzene bond	0·667	
p_{ab} : 2 : 3-bond in phenanthrene	0·623	$\delta_{ab} = -0{\cdot}066$
p'_{ab} : 3 : 4-bond in diphenyl	0·660	$\delta'_{ab} = -0{\cdot}010$

$$L_0 = -1{\cdot}065\beta.$$

These values when inserted into (7) give $L = -1{\cdot}024\beta$; the last digit is probably not reliable since the relationships (5) and (6) are statistical in nature. For comparison, the value of L calculated by a more direct (but also approximate) method is $-1{\cdot}030\beta$, where again the last digit is probably not significant.

The most important application of (7) is, however, to determine qualitatively whether annelation increases or decreases the reactivity of Y. Evidently, since L represents an activation energy, the reactivity is decreased when $p_{ab} > p'_{ab}$ and *vice versa*, so the change in reactivity of Y due to annelation to its $a:b$-bond can be discussed simply in terms of the mobile orders of this bond and the corresponding bond in the residual molecule. *The qualitative result*

is independent of the nature of X. In the example considered above, the qualitative result that the 3 : 4-bond of benzanthracene is more reactive than the 9 : 10-bond of phenanthrene could have been predicted from the fact that the 3 : 4-bond of diphenyl has a greater mobile order than the 2 : 3-bond of phenanthrene, X being assumed to be benzene. The same data, X now being assumed to be naphthalene, lead to the result that the most reactive bonds in 1 : 2-5 : 6-dibenzanthracene, 1 : 2-7 : 8-dibenzanthracene, and 1 : 2-benzonaphthacene are more reactive than the 9 : 10-phenanthrene bond. Similarly, we expect the 1 : 2-bond of chrysene to be less reactive than this phenanthrene bond because the mobile order of the 1 : 2-bond of phenanthrene (0·705) is greater than that of the 3 : 4-bond of diphenyl. In view of the rather extensive mobile-order data available in the literature, together with some simple methods for judging qualitatively the relative mobile orders of bonds, this principle should prove very useful for qualitative predictions, particularly for the Diels–Alder and osmium tetroxide reactions.

The relation analogous to (7) for $L' - L'_0$, *i.e.*, with the inclusion of the overlap integral, can be written down from the relationships corresponding to (5) and (6) for K' (Brown, *Trans. Faraday Soc.*, *loc. cit.*). It differs from (7) in that the numerical constant 1·077 is now replaced by 1·034 and that the energy unit β is replaced by γ. The equation may be employed to estimate the relative rate constants for reaction of the two compounds

$$k/k_0 = \exp[(L'_0 - L')/\boldsymbol{R}T)$$

It is again convenient to use the osmium tetroxide reaction as an example because experimental relative-rate data are available for this reaction (Badger and Reed, *Nature*, 1948, **161**, 237; Badger, *J.*, 1949, 456). For 20° and $-\gamma = 34$ kcals. we have

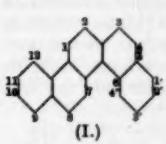
$$k/k_0 = \exp\{60_3\,(p'_{ab} - p_{ab})[1 - (\delta_{ab} + \delta'_{ab})/4]\}. \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

expressing the reaction-rate-constant contribution from a particular bond in the YX compound relative to that of the corresponding bond in Y in the particular case of the osmium tetroxide reaction.

As the first example, we may take phenanthrene and benzanthracene, already considered above. From (8) we derive $k/k_0 = 8$ for the reaction-rate constant of the 3 : 4-bond of benzanthracene relative to the 9 : 10-bond of phenanthrene. These bonds are far more reactive than any others in their respective molecules so this figure will also represent the relative reaction-rate constants for the two molecular species. The value found experimentally by Badger and Reed (*loc. cit.*) is 10. It will be noticed that k/k_0 is an exponential function of the quantity $p' - p$, so that agreement even in order of magnitude is to be regarded as satisfactory.

Another important example is provided by the pair benzanthracene and 1 : 2-5 : 6-dibenzanthracene. It is found on inserting the appropriate values into (8), and assuming that p'_{ab}, the mobile order of the 5 : 6-bond in 2-phenylnaphthalene, is the same as in unsubstituted naphthalene, that k/k_0 for the 3 : 4-bonds of these two hydrocarbons comes to 0·63. However, the annelation of a benzene ring to the 5 : 6-bond of benzanthracene produces another bond equivalent to the 3 : 4-bond of dibenzanthracene. These two bonds are far more reactive than all others in dibenzanthracene, so the relative molecular rate constants for benzanthracene and dibenzanthracene will be $0{\cdot}63 \times 2 = 1{\cdot}3$. This is in excellent agreement with the experimental value of 1·3 (Badger, *loc. cit.*). Here we have the interesting case of the 3 : 4-bond of benzanthracene being deactivated by annelation, and in spite of this the resultant molecule is more reactive than benzanthracene owing to the formation of another equivalent reactive bond.

It is apparent that a complication arises when the annelation gives rise to other bonds of reactivity comparable with the one under consideration, especially when they are not equivalent to it by symmetry, as they happen to be in the case just considered. However, even in these cases it is usually possible to determine k/k_0 for all reactive bonds in the molecule such that k_0 represents the bond rate constant of either the phenanthrene 9 : 10-bond or the benzanthracene 3 : 4-bond. The procedure again is best illustrated by an example. We shall calculate the molecular rate constant for 5 : 6-benzochrysene (I) relative to phenanthrene. It is apparent from general considerations (Brown, *J.*, 1950, 3249) that the only bonds sufficiently reactive to be considered are 1 : 2, 3 : 4, and 7 : 8. To consider, first, the reactivity of the 3 : 4-bond relative to phenanthrene, we regard benzochrysene as formed by annelation of the 1 : 2-bond of naphthalene to the 3 : 4-bond of phenanthrene. Substitution of the appropriate values in (8) yields $k/k_\gamma = 0{\cdot}21$, where we have written k_γ to indicate that the 9 : 10-phenanthrene bond is being used as reference point. Similarly, the reactivity of the 7 : 8-bond is treated by regarding benzochrysene as formed by



(I.)

fusion of the 1 : 2-bond of naphthalene to the 1 : 2-bond of phenanthrene. This time we find $k/k_p = 0{\cdot}06$. The reactivity of the 1 : 2-bond can be found first by finding the reactivity of the 1 : 2-bond of chrysene relative to phenanthrene and then the change in its reactivity due to annelation of a benzene ring to the 5 : 6-chrysene bond. However, little error is introduced in treating benzochrysene as 1 : 2-5 : 6-dibenzophenanthrene and assuming that the effect of the two annelations upon the 9 : 10-phenanthrene bond is additive. This is easily seen to be equivalent to assuming that the relative rate constant for the 1 : 2-bond of 5 : 6-benzochrysene is the product of relative rate constants for the 1 : 2-bond of chrysene and the 1 : 2-bond of 3 : 4-benzophenanthrene. In the latter way we obtain $k/k_p = 0{\cdot}016$, but in view of the approximations invoked this cannot be taken to indicate more than order of magnitude. To obtain the molecular relative rate constant we sum over all bonds of the molecule. As mentioned above, the only significant contributions come from the three bonds just considered, and we conclude that the relative rate constant for benzochrysene is 0·3. Unfortunately, the value has not yet been determined experimentally.

One possible limitation to the use of equations (7) and (8) must be mentioned. The annelation relationships (5) and (6) have only been investigated for alternant hydrocarbons, *i.e.*, hydrocarbons containing only even-membered rings; it has not yet been determined if they are still valid for hetero-molecules or for radical systems. Consequently, at present we can apply (7) and (8) with confidence only to reactions for which both the original molecule and the residual molecules are hydrocarbon systems. Reactions for which this is true are the Diels–Alder reaction and the reaction with osmium tetroxide.

Hetero-atoms.—Another problem of importance is to predict the change in reactivity of a conjugated system, Y, when one of its carbon atoms is replaced by a hetero-atom such as nitrogen. Suppose it is the ith atom that is replaced by a hetero-atom. We may write the π-electron energy of the resultant molecule as

$$\mathbf{E} = \mathbf{E}_0 + \mathbf{W}_i \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

where $\mathbf{E}_0$ is the π-energy of Y, and we may take (9) as defining $\mathbf{W}_i$, which will be termed the perturbation energy, and for a given hetero-atom will in general depend upon which atom, i, is replaced.

A similar expression may be written for $\mathbf{E}'$, so that we can immediately derive

$$\mathbf{L} - \mathbf{L}_0 = \mathbf{W}_i' - \mathbf{W}_i \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

If we now consider the L.C.A.O. molecular-orbital approximations to the various quantities appearing in (10), it is possible to put the right-hand side into a more convenient form. The major effect of the replacement of the ith carbon atom by a hetero-atom is to alter its coulomb term, α_i. We can then expand E and E' as a Taylor series in $\delta\alpha_i$ and thus obtain

$$W_i = \delta\alpha_i[\mathrm{d}E/\mathrm{d}\alpha_i + (\mathrm{d}^2E/\mathrm{d}\alpha_i^2)(\delta\alpha_i)/2 + \ldots] \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

with an analogous expression for W_i'. It is convenient to write $h_i\beta$ for $\delta\alpha_i$, β being the resonance integral, and to make the usual assumption that h_i depends upon the nature of the hetero-atom only and not upon i. The differential coefficients in (11) are just the charge, q_i, and self-polarisability, $\pi_{i,i}$, of position i (Coulson and Longuet-Higgins, *Proc. Roy. Soc.*, 1947, *A*, **191**, 39). These may be inserted into (11) and the corresponding expression for W_i', and the results incorporated into (10) to give

$$L - L_0 = h\beta[(q_i' - q_i) + (\lambda_i' - \lambda_i)h/2 + \ldots] \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

where λ_i, a pure number, has been written for $\beta\pi_{i,i}$.

Equation (12) is simplified further if the original or residual molecule or both are alternant hydrocarbons, since for these latter all the q_i are unity (Coulson and Rushbrooke, *Proc. Camb. Phil. Soc.*, 1940, **36**, 193).

Longuet-Higgins (*J. Chem. Physics*, 1950, **18**, 283) has discussed some aspects of substitution reactions of aromatic and heterocyclic systems, using the equivalent of equation (12) but retaining only the first term, $q' - q$. However, another interesting application of (12) is to reactions such as the Diels–Alder reaction and osmium tetroxide reaction where, if the original molecule is an alternant hydrocarbon, then so also is the residual molecule. If we retain only the first non-vanishing term in (12), we have for these reactions

$$L - L_0 = (-\beta)(\lambda_i - \lambda_i')h^2/2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (13)$$

To illustrate the order of magnitude of the changes in reactivity predicted by (13) some values are given in Table I. The self-polarisabilities have been taken from the literature (Coulson

TABLE I.

Reactivities of aza-hydrocarbons relative to parent hydrocarbons.

(*a*) Osmium tetroxide reaction at the 9 : 10-bond.

	Position.	$L - L_0$.*		Position.	$L - L_0$.*
1-Azaphenanthrene		-0.022β	3-Azaphenanthrene		-0.005
2-Azaphenanthrene		$+0.004$	4-Azaphenanthrene		-0.003

(*b*) The Diels–Alder reaction.

Quinoline	1 : 4	-0.023β	3'-Aza-1 : 2-benzanthracene	9 : 10	$+0.001$
*iso*Quinoline	1 : 4	$+0.048$	4'- ,,	9 : 10	$+0.002$
	5 : 8	-0.004	3- ,,	9 : 10	-0.002
1-Aza-anthracene	9 : 10	-0.028	4- ,,	9 : 10	-0.021
2- ,,	9 : 10	-0.006	6- ,,	9 : 10	-0.027
1'-Aza-1 : 2-benzanthracene	9 : 10	$+0.002$	7- ,,	9 : 10	-0.005
2'- ,,	9 : 10	-0.003	8- ,,	9 : 10	-0.025

* It is assumed for convenience that $h = 1$.

and Longuet-Higgins, *Proc. Roy. Soc.*, 1948, *A*, **195**, 188; Brown, *Experientia*, 1950, **6**, 376; Greenwood, unpublished results).

It seems likely that for nitrogen h is not greater than unity, and that higher terms in the expansion (12) are less important than the first two, so the values given in Table I for $L - L_0$ are likely to be at least qualitatively correct. The values, which are listed assuming $h = 1$, are all very small, the greatest change in reactivity being for 1 : 4 Diels–Alder addition to *iso*quinoline compared with naphthalene. This figure probably corresponds to relative rate constants of 10 : 1 for the 1 : 4-positions in the respective molecules, and since naphthalene has two equivalent pairs of positions and the 5 : 8-positions of *iso*quinoline are similar in reactivity to the 1 : 4-naphthalene positions, the tabulated value would indicate that *iso*quinoline should react about six times as rapidly as naphthalene with, say, maleic anhydride.

The results presented in Table I, and similar results for other systems, have more important uses than this, however. If a position in a hydrocarbon could be found for which $\lambda_i - \lambda_i^0$ is unusually large, then the relative rates of reaction of the hydrocarbon and the corresponding aza-hydrocarbon found experimentally could be employed to determine $h^2\beta$ for nitrogen. The resonance integral β likewise could be determined from experimental relative rate constants for pairs of hydrocarbons, pairs for which (7) is applicable being particularly appropriate. This affords an experimental means for determining the parameter h. There may, however, be complicating factors, one of which must now be considered in connection with another use for the data of Table I.

It is sometimes suggested (Badger, *J.*, 1950, 1809) that the reactivity of a bond towards osmium tetroxide is partly determined by the charges at either end of the bond. At present there is no satisfactory experimental evidence to support this suggestion and some theoretical evidence (Brown, *J.*, 1951, 1950) against it. However, a hetero-molecule will have in general a relatively large dipole moment compared with its parent hydrocarbon, so there will be a stabilization of the activated complex of the former relative to that of the latter owing to induction forces involving the dipole moment of the heterocyclic system and the polarisable electrons of the osmium tetroxide, similar to the forces responsible for the difference in stability of the *endo*- and *exo*-forms of Diels–Alder adducts (cf. *idem*, *ibid.*, p. 1612). Qualitatively, such effects would be expected to increase the reactivity of hetero-molecules compared with their parent hydrocarbons by a greater amount than that predicted by (13). Consequently, experimental investigation of reactivities of hetero-molecules should serve to throw more light both upon the theoretical treatment of such systems and upon the mechanism of bond reactions. Badger and Lyon's measurement of the rate of reaction of methyldibenzacridine with osmium tetroxide (*J.*, 1950, 1726) indicates little difference in reactivity from the corresponding methylbenzanthracene. Since we should expect theoretically that this latter compound would have very similar reactivity to the methyldibenzanthracene, this measurement points to an insignificant influence of the hetero-atom on the reactivity, as would be expected from the results of Table I. This suggests in turn that the polarity of the hetero-molecule plays little part in its reactivity, but clearly a more thorough experimental investigation is still needed.

Similar remarks apply to the Diels–Alder properties of hetero-molecules. In this case there is the possibility of quantitative studies of equilibria to determine the parameter h. Perhaps the most interesting result in Table I is the increased Diels–Alder reactivity of the 1 : 4-positions in *iso*quinoline compared with naphthalene, in view of the recently reported formation of an

adduct of the latter with maleic anhydride (Kloetzel and Herzog, *J. Amer. Chem. Soc.*, 1950, **72**, 1991). The other conclusion to be drawn generally from (13) is that from the standpoint of preparative organic chemistry if a certain hydrocarbon adds maleic anhydride then so will all its aza-derivatives (excepting cases where the nitrogen atom occupies one of the positions which would normally undergo addition). Some isolated examples appear in the literature; *e.g.*, Huisgen (*Annalen*, 1949, **564**, 16) has reported Diels–Alder reactivity of a substituted 1-aza-anthracene. Since substituents have a relatively small effect upon bond or Diels–Alder reactivity unless they are at one of the reactive positions (to be discussed in Part II) the present theory predicts reactivity for a large number of reported heterocyclic derivatives. As a representative example may be quoted the derivatives of 2 : 3-benzacridine reported by Cairns and Kermack (*J.*, 1950, 1322).

In the above discussion of heterocyclic systems it has been supposed that the predominant effect of the hetero-atom is to perturb the Coulomb term of the carbon atom it replaces. However, it seems likely that the resonance integrals of all bonds ending at the hetero-atom will also be perturbed. The effect of these perturbations is to add to the right-hand side of (11) the additional Taylor series

$$\delta\beta\{\Sigma_j \partial E/\partial\beta_{ij} + \tfrac{1}{2}\Sigma_j\Sigma_k\,(\partial^2 E/\partial\beta_{ij}\partial\beta_{ik})\delta\beta + \ldots\} \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

where the summations are over all atoms adjacent to the hetero-atom at i. If we write for convenience the perturbation $\delta\beta$ as $k\beta$ and use the identities of the differential coefficients with mobile bond orders and self-bond polarisabilities (Coulson and Longuet-Higgins, *loc. cit.*) (14) becomes

$$k\beta(\Sigma_j 2p_{ij} + \Sigma_j\Sigma_k \pi_{ij,ik}\,k\beta + \ldots..). \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (15)$$

p_{ij} being the mobile order of the $i : j$ bond and $\pi_{ij,ik}$ being the mutual polarisability between bonds $i : j$ and $i : k$. Strictly we should also add to (11) a series of cross terms, the first of which is $\Sigma_j\ \pi_{i,ij}\ k^2\beta^2$, but for alternant hydrocarbons the atom-bond polarisabilities, $\pi_{i,ij}$, are identically zero, and since k is small (see below) the term will be unimportant in other cases.

The expression for the change in localization energy then becomes

$$\begin{aligned} L - L_0 = {} & k\beta[(q_i^2 - q_i) + (\lambda_i^2 - \lambda_i)k/2 + \ldots.] \\ & + k\beta[2(F_i - F_i^0) - (Y_i^2 - Y_i^0)k + \ldots.] \quad . \quad . \quad . \quad . \quad . \quad . \quad (16) \end{aligned}$$

where F_i is the free valency of position i and Y_i is a dimensionless function of the mutual bond polarisabilities. For the usual case when the hetero-atom replaces a carbon atom, i, with two neighbours, a and b, it is

$$Y_i = (\pi_{ai,ai} + 2\pi_{ai,bi} + \pi_{bi,bi})\beta$$

In particular, when the hetero-atom is nitrogen, k is probably very small (cf. Longuet-Higgins and Coulson, *Trans. Faraday Soc.*, 1947, **43**, 87) and may be considerably less than 0·1. Furthermore, for most positions in alternant hydrocarbons Y_i is of the order 0·1, so the second term in

TABLE II.

The effect of perturbation of the resonance integral.

Osmium tetroxide reaction at 9 : 10-bond.

	$F_i - F_i^0$.
1-Aza-phenanthrene	0·057
2- ,, ...	0·008
3- ,, ...	0·012
4- ,, ...	0·003

Diels–Alder reaction.

	Position.	$F_i - F_i^0$.
Quinoline	5 : 8	0·053
*iso*Quinoline	1 : 4	0·328
	5 : 8	0·005
1-Aza-anthracene	9 : 10	0·060
2-Aza- ,, ...	9 : 10	0·009
3-Aza-1 : 2-benzanthracene	9 : 10	0·004
4-Aza- ,,	9 : 10	0·051

the second series in (16) will usually be quite negligible. To illustrate the importance of the first term of the second series, values of $F_i - F_i^0$ are given in Table II for some of the compounds considered in Table I. It is clear that, apart from the exceptional case of 1 : 4-addition to *iso*quinoline, where in any case the assumption of constancy in σ-bond energy changes is likely to break down, the effect of the first term of the second series will be negligible compared with that of the second term of the first series owing to the small value of k.

Equation (12) or the more general equation (16) should apply for all reactions which can be treated by the localization theory, not only the Diels–Alder and osmium tetroxide reactions. Unfortunately, the familiar substitution reactions of conjugated systems involve radical residual molecules for which self- and mutual-atom- and bond-polarisabilities are not available

in the literature, so one has to be content at present with the elegant qualitative treatment by Longuet-Higgins (*J. Chem. Physics*, 1950, **18**, 283) using only the first term in (16), *i.e.*, $q_i' - q_i$.

The above work was carried out during tenure of an Australian National University Travelling Scholarship. The author is grateful to Professor C. A. Coulson, F.R.S., for the opportunity of discussing the manuscript with him and to Mr. H. H. Greenwood for communicating polarisability data for benzanthracene before publication.

THEORETICAL PHYSICS DEPARTMENT,
KING'S COLLEGE, STRAND, LONDON, W.C.2. [*Received, March 29th*, 1951.]

---

439. *The Configuration of Flexible Polymethylene Molecules in the Gas Phase.*

By J. C. MCCOUBREY, J. N. MCCREA, and A. R. UBBELOHDE.

Published data on the viscosities of gaseous hydrocarbons in the range 20—200° have been supplemented by new determinations, at various temperatures, for *iso*pentane, *cyclo*pentane, *n*-hexane, benzene, hex-1-ene, methyl*cyclo*pentane, *n*-, *iso*-, and *cyclo*-octane. Molecular volumes of the liquids at their boiling points have also been determined. By a survey of all the data and of entropies of vaporisation of the liquids at their boiling points, the conclusion reached is that the average molecular configuration of the flexible *n*-C_5—C_8-hydrocarbons in the vapour phase is quite highly coiled.

WHEN sufficiently large potential barriers oppose a change of shape, as in certain *cyclo*hexane derivatives, or in unsaturated *cis–trans*-isomers, experiments on molecular configurations can be carried out by actual segregation of the different species, by using the standard techniques available for investigation of isomerism.

However, for problems of reaction mechanism, and for other problems of chemical physics, a knowledge of the average configuration of a molecule is required even in cases where the change of shape occurs too rapidly for any separation of the different configurations to be feasible. As a rough distinction for experimental convenience, molecular configurations with a half life of the order of one hour or less under the conditions of experiment may be termed "flexible." Normally these must be investigated from averaged properties of a mixture of molecules of different configurations.

Much theoretical and experimental work has been published recently on the average configuration in solutions of flexible molecules of high polymers. But statistical methods which are successful when the number of flexible units in a chain molecule is large do not offer the same scope when there are comparatively few units in the molecule. Information on the shorter polymethylene chains is relevant, for example, in problems of the influence of structure on the reactivity of such molecules in the gas phase (Ubbelohde, *Rev. Inst. Franç. du Pétrole et Ann. Combust. liq.*, 1949, **4**, 488; McCoubrey and Ubbelohde, *Faraday Soc. Discuss.*, 1951). A convenient nomenclature is to describe the flexible molecules in their fully stretched zig-zag configuration as *trans*. As each C–C bond is rotated to the *cis*-position the coiling of a polymethylene molecule increases progressively.

The present paper records experimental results which yield information about the average configuration of polymethylene molecules in the range C_4—C_8. Earlier, rather scattered determinations of the viscosities, at various temperatures, of the vapours of *n*- and *iso*-butane, *n*-pentane, benzene, *n*- and *cyclo*-hexane, *n*-heptane, and *n*-octane have been supplemented by redeterminations in the case of benzene, *n*-hexane, and *n*-octane. New results have also been obtained for *iso*- and *cyclo*-pentane, hex-1-ene, methyl*cyclo*pentane, and *iso*- and *cyclo*-octane, in order to permit comparisons between structurally related compounds.

As discussed below, no fully worked out kinetic theory of momentum transfer is yet available for such flexible molecules. However, a comparison of calculated kinetic parameters within a series of structurally related compounds shows that polymethylene hydrocarbons up to C_8 behave, in homomolecular collisions, predominantly as coiled molecules. This conclusion is compared with inferences based on parameters of the molecules not directly dependent on collisions, by use of new measurements of the molecular volumes of the liquids at their boiling points.

These measurements, and data on the entropies of vaporisation, confirm that on average the external aspect of molecules of *n*-paraffins in the gas phase is much the same as that of fully

branched isomers, so that the *n*-paraffins behave as if they were quite highly coiled in the gas phase, *i.e.*, as if many of the C–C bonds were on average far from the *trans*-configuration.

Experimental.

Materials (cf. Table I).—Samples were purified where necessary by carefully controlled fractionation in a 12" column packed with glass helices (10—12 plates). The redistilled liquids were then carefully dried by bubbling dry oxygen-free nitrogen through them near the b. p.s. Final purification was by distillation within the apparatus. Before such a distillation the liquid was frozen repeatedly in liquid air and allowed to melt *in vacuo*, to expel permanent gases; this precaution appears to be particularly important when capillary methods are used in viscosimetry.

Table I.

Characteristics of materials used.

Hydrocarbon.	Ref.	Boiling range, ± 0·1°.	n_D^{20}.*	*d*.	Mol. vol. at b. p., ml.	Mol. entropy of vaporisation at b. p., e.u. (ref. 2).
n-Butane	2	—	—	—	—	19·63
*iso*Butane	2	—	—	—	—	19·47
n-Pentane	1	37·0°	1·3575	0·610 ± 0·001	118·2	19·92
*iso*Pentane	1	28·0	1·3536	0·612 ,,	117·8	19·41
*cyclo*Pentane	1	49·2	1·4056	0·713 ,,	101·1	20·26
n-Hexane	1	68·3	1·3743	0·615 ,,	140·0	20·17
Hex-1-ene	1	63·5	1·3866	0·643 ,,	133·9	—
*cyclo*Hexane	1	80·7	1·4263	0·719 ,,	116·9	20·30
Methyl*cyclo*pentane	1	71·5	1·4095	0·699 ,,	120·3	20·30
Benzene	1	80·1	1·5008	0·814 ,,	95·0	20·81
n-Heptane	1	98·2	1·3875	0·615 ,,	162·6	20·36
2 : 2-Dimethylpentane	2	—	—	—	—	19·54
n-Octane	1	125·5	1·3974	0·616 ,,	185·3	20·96
2 : 2 : 4-Trimethylpentane	1	99·0	1·3912	0·625 ± 0·002	182·6	19·90
*cyclo*Octane	1	147·5	1·4588	0·744 ± 0·002	150·7	—

[1] Present experiments. [2] Bur. Stand. Amer. Petroleum Res. Project 44.
* Determined on a Hilger–Abbé refractometer.

Thanks are offered to the Anglo-Iranian Oil Company for gifts of *n*-, *cyclo*-, and *iso*-pentane, *n*-hexane, and 2 : 2 : 4-trimethylpentane (*iso*octane), to Distillers Company Ltd. for gifts of *cyclo*pentane and methyl*cyclo*pentane, and to the British Oxygen Company for a gift of *cyclo*octane. Hex-1-ene was obtained from Messrs. Light's, and *n*-octane (synthetic) from B.D.H. The benzene used was as purified for freezing-point measurements (Thompson and Ubbelohde, *Trans. Faraday Soc.*, 1950, **46**, 349).

The Molecular Volume at the Boiling Point.—To determine the density of the liquid hydrocarbon, a 0·5-ml. Pyrex pyknometer was calibrated with water. This pyknometer was then filled with a hydrocarbon and was suspended in the vapour at the b. p. The mass of liquid was found by then cooling and weighing the pyknometer. The method was checked by a number of experimental determinations with benzene. Standard precautions (cf. Burroughs, *Bur. Stand. J. Res.*, 1928, **1**, 635) were taken to ensure that the pyknometer was at the temperature of liquid–vapour equilibrium, and generally three determinations were made with each liquid. Results are recorded in Table I. Where comparisons could be made, the values agreed within 0·001 g./ml. with extrapolated I.C.T. values, further verifying the purity of the samples.

Viscosities.—The capillary viscometer used was basically similar to that described by Rankine (*Proc. Roy. Soc.*, 1913, **88**, 575) and Nasini (*ibid.*, 1929, **123**, 686); only major additions and improvements are described in Fig. 1. These included direct and continuous pressure measurement on both sides of the capillary by means of two Pyrex-spiral pressure gauges fitted with optical levers. The pressures of air required to bring the spirals back to the null point were read on a mercury manometer to 0·1 mm. Special experiments on the vapour pressure above the liquid in the tube during a run showed that the effective driving pressures were always less than the equilibrium vapour pressures at the bath-temperatures. By inserting a silver wire upwards through the column of liquid into the vapour much closer approximation of driving pressures to equilibrium vapour pressures could be obtained. Extremely vigorous stirring (using a magnetic plunger operated by a permanent magnet outside the tube) produced considerable splashing of the liquid and also gave good agreement between the driving pressures and the equilibrium vapour pressures. Actual behaviour in the absence of these precautions corresponded with a drop in temperature of about 1·5° at 50 mm. pressure on passage from the body of the liquid to the surface. Neither of the above methods was convenient for use in systematic measurements on the rate of transfer of mass through the capillary, so that continuous readings were taken of the actual driving pressure. The bath-temperature around the graduated tube was controlled to ±0·025°. The portion of this tube (a 1-c.c. Pyrex pipette) which was used in the runs had a constant radius of 0·1085 cm., measured by calibration with mercury. The fall in the liquid level during capillary flow was measured at intervals to ±0·01 mm. with a cathetometer. After passing through the capillary the vapours were condensed in liquid air. The spiral gauge generally showed that the pressure on this side was negligible. The temperature of the bath oil around the capillary was maintained electrically to ±0·25°. The capillary tube was a "Veridia" capillary supplied by Chance Brothers. Calibration with a mercury pellet showed that it had a uniform diameter of $0{\cdot}992 \times 10^{-3}$ cm. ± 0·03% over the length used (*ca.* 20 cm.). In the calculations which follow, no correction has been made for possible effects of multi-

layer absorption on the effective diameter of the capillary, or on the slip correction. Multilayers thicker than 5×10^{-4} cm. could have an appreciable effect in decreasing flow and thus increasing the apparent viscosity.

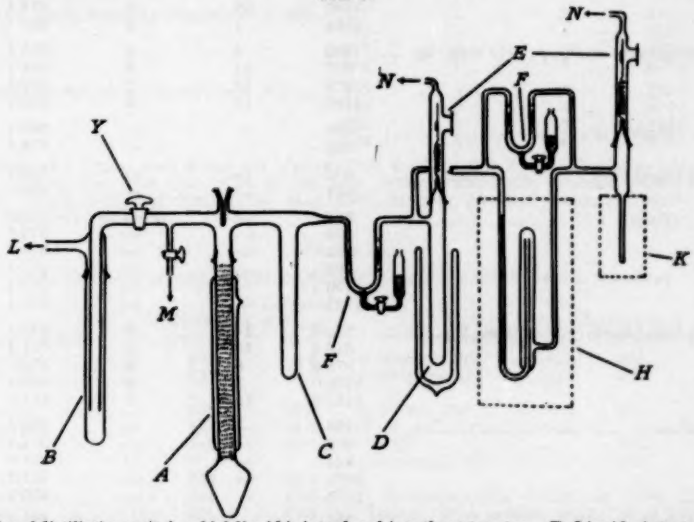
To avoid *ad hoc* end corrections, the resistance of the viscometer was calibrated with dry air. For this purpose a volume of about 6 l. of air at measured pressure was connected to one side of the capillary, and the other side was kept effectively at zero pressure by continuous pumping.

By use of the values $\eta_{288} = 1795 \times 10^{-7}$ and $\eta_{273} = 2171 \times 10^{-7}$ c.g.s units (temp. are K.) for air (Johnson and McCloskey, *J. Phys. Chem.*, 1940, **44**, 1038), the average of four independent determinations at each temperature was found to be $r^4/L = 389{\cdot}8 \times 10^{-12}$ with a mean deviation of $\pm 0{\cdot}4\%$. In calculating viscosities the standard Poiseuille equation was used, *viz.*:

$$\eta = \frac{r^4}{L} \times \frac{p_1^2 - p_2^2}{16} \times \frac{273\rho}{760T} \times \frac{t}{m}$$

where m is mass transpired in time t seconds (measured in terms of the volume of liquid evaporated), ρ is the density of vapour at N.T.P., T is the capillary temperature in °K., p_1 and p_2 are the pressures (dynes/cm.²) on either side of the capillary, r is the radius of the capillary, and L is its length in cm. η is the coefficient of viscosity.

FIG. 1.



A, *Fractional distillation unit, in which liquid is introduced into the apparatus.* B, *Liquid-air trap.* C, *Tube for bulb-to-bulb distillation from* C *to* D. D, *Condensation point for vapours after they pass through the capillary.* E, *Pyrex-spiral pressure gauges.* F, *Mercury-seal taps.* H, *Capillary arrangement, showing preheater and surrounding thermostat bath.* K, *Graduated tube, with thermostat bath.* L, *Lead to Hyvac rotary and diffusion pumps.* M, *Lead to manometric system, by means of which the pressure inside the apparatus can be measured during fractionation.* N, *Leads to manometric system, so that the air pressure inside the gauge jackets can be measured.*

By way of illustration data for *cyclo*pentane are recorded in detail (Table II).

TABLE II.

Flow data for cyclo*pentane.*

Temp. of capillary.	*d.*	Drop in liq. level, cm./hr.	Driving pressure, cm. Hg.	η, poises.	η, corr. for slip, poises.	Temp. of capillary.	*d.*	Drop in liq. level, cm./hr.	Driving pressure, cm.Hg.	η, poises.	η, corr. for slip, poises.
18·5°	0·765	5·490	9·55	826	845	109·0	0·773	2·850	8·80	1021	1044
18·5	0·765	5·400	9·55	837	853	109·0	0·773	2·850	8·75	1010	1033
18·5	0·765	5·620	9·75	830	846	109·0	0·773	2·370	8·00	1015	1038
19·0	0·765	5·700	9·65	811	828	140·0	0·773	2·260	8·40	1085	1114
19·0	0·765	5·900	9·65	784	801	140·0	0·773	2·040	7·86	1050	1079
76·0	0·763	4·800	10·60	973	997	140·0	0·773	1·950	7·70	1059	1086
79·0	0·767	4·220	9·90	952	970	140·0	0·773	2·310	8·60	1113	1142
75·0	0·765	4·400	10·10	966	984	176·0	0·773	2·160	8·75	1133	1164
109·0	0·773	2·760	8·71	1031	1054	176·0	0·775	2·600	9·60	1134	1163

TABLE III.

Summarised viscosity data.

	η, poises.	Precision (±).	No. of independent observations.	Temp. (K.).	$\mathfrak{A}$.
n-Butane (Titani)	739	—	—	293·1	0·177
	787	—	—	323·1	0·174
	947	—	—	373·1	0·155
	998	—	—	393·1	0·151
*iso*Butane (Titani)	744	—	—	293·1	0·175
	792	—	—	323·1	0·173
	947	—	—	373·1	0·155
	995	—	—	393·1	0·152
*cyclo*Pentane (present work), p_1 ~90 mm. Hg	835	16	5	292·6	0·171
	985	9	3	352·1	0·159
	1042	7	4	382·1	0·157
	1105	23	5	413·1	0·154
	1164	1	2	449·1	0·152
*iso*Pentane (present work), p_1 ~75 mm. Hg	693	8	4	291·1	0·209
	807	11	3	341·1	0·194
	978	13	3	415·1	0·177
	1108	14	4	453·1	0·163
,, (Bleakney)	695	—	—	298·1	0·211
	860	—	—	373·1	0·191
n-Pentane (Bleakney)	676	—	—	298·1	0·217
	841	—	—	373·1	0·195
,, (Titani)	662	—	—	298·1	0·221
	868	—	—	373·1	0·189
	911	—	—	395·1	0·185
	995	—	—	432·1	0·177
	1126	—	—	492·1	0·167
	1191	—	—	523·1	0·163
Benzene (present work), p_1 ~70 mm. Hg	744·7	14	5	295·1	0·204
	846·1	10	4	327·1	0·189
	979·3	6	4	374·1	0·174
	1030·0	5	3	406·1	0·173
	1134·4	18	5	451·1	0·165
,, (Nasini)	736	—	—	289·1	0·204
	802	—	—	314·1	0·195
	941	—	—	373·6	0·181
	1074	—	—	423·1	0·169
	1176	—	—	470·3	0·163
,, (Titani)	738	—	—	281·1	0·203
	918	—	—	323·1	0·173
	1031	—	—	403·1	0·172
	1110	—	—	434·1	0·166
	1198	—	—	468·1	0·160
n-Hexane (present work) p_1 ~68 mm. Hg	614·3	4	5	288·1	0·256
	737·6	8	3	349·1	0·235
	796·2	2	3	376·1	0·286
	835·0	9	5	395·1	0·221
	904·6	5	3	423·1	0·211
	981·1	8	4	462·1	0·203
,, (Titani)	866	—	—	394·1	0·213
	958	—	—	434·1	0·226
	1021	—	—	462·1	0·195
Hex-1-ene (present work), p_1 ~68 mm. Hg	681·1	10	5	301·1	0·234
	772·5	3	5	348·1	0·221
	902·8	9	3	398·1	0·203
	931·6	6	5	419·1	0·202
	1000·2	5	5	450·1	0·195
Methyl*cyclo*pentane (present work), p_1 ~85 mm. Hg	762	14	6	293·1	0·206
	837	6	4	341·9	0·203
	891	13	5	378·7	0·200
	1019	16	3	414·6	0·183
	1097	10	5	450·5	0·177

TABLE III—*continued.*

	η, poises.	Precision (±).	No. of independent observations.	Temp. (K.).	Ω.
n-Heptane (Melaven and Mack)	717	—	—	373·1	0·270
	811	—	—	423·1	0·254
	922	—	—	475·1	0·237
	1080	—	—	524·1	0·212
2 : 2-Dimethylpentane (Melaven and Mack) ...	734	—	—	343·1	0·253
	769	—	—	374·1	0·252
	827	—	—	405·1	0·244
	900	—	—	449·1	0·236
	1048	—	—	535·1	0·221
n-Octane (present work), p_1 ~20 mm. Hg	689	19	8	379·5	0·302
	762	2	3	419·4	0·287
	800	18	8	446·7	0·282
	875	3	3	473·8	0·266
2 : 2 : 4-Trimethylpentane (present work), p ~35 mm. Hg	727	12	3	374·8	0·285
	770	11	3	402·1	0·278
	817	15	5	433·4	0·272
	898	17	2	467·1	0·257
*cyclo*Octane (present work), p_1 ~20 mm. Hg ...	703	4	2	398·6	0·301
	708	19	4	414·1	0·304
	755	7	3	442·6	0·295
	805	6	4	478·1	0·288

References: Titani, *Bull. Chem. Soc. Japan*, 1929, **4**, 277; 1930, **5**, 98; Bleakney, *Physics*, 1932, **3**, 123; Nasini, *Proc. Roy. Soc.*, 1929, *A*, **123**, 692; Melaven and Mack, *J. Amer. Chem. Soc.*, 1932, **54**, 888; Titani, quoted by Schuil, *Phil. Mag.*, 1939, **28**, 679; Everhart, Hare, and Mack, *J. Amer. Chem. Soc.*, 1933, **55**, 4894.

TABLE IV.

Interpretation of temperature coefficients of viscosity (Sutherland's equation).

Hydrocarbon.	Sutherland's constant.	Collision area, A, sq.A.	Hydrocarbon.	Sutherland's constant.	Collision area, A, sq.A.
n-Butane (T)	358	16·6	*n*-Heptane (M)	445	26·7
*iso*Butane (T)	330	17·1	*iso*Heptane (E)	257	31·1
n-Pentane (T)	383	19·6	*n*-Octane (W)	577	28·2
*iso*Pentane (W)	468	19·2	2 : 2 : 4-Trimethylpentane (W)	394	32·9
*cyclo*Pentane (W)	140	27·0	*cyclo*Octane (W)	205	47·0
Benzene (W)	344	22·1			
n-Hexane (W)	384	25·6			
Hex-1-ene (W)	392	23·8			
*cyclo*Hexane (T)	351	21·2			
Methyl*cyclo*pentane (W) ...	293	24·3			

References (for details see Table III): T = Titani; W = present work; M = Melaven and Mack; E = Everhart *et al.*

The Poiseuille value of η was corrected for slip by means of the standard formula $\eta_{corr.} = \eta(1 + 4\eta/\varepsilon r)$, where the slip coefficient η/ε is given by

$$\eta/\varepsilon = \frac{1{\cdot}70\sqrt{3RT/M}}{(p_1 + p_2)}$$

where M is molecular weight and the other symbols have their usual meanings. The numerical values of $(\eta_{corr.} - \eta)$ at the pressures and temperatures used ranged from 1 to 4% of η.

The correction for non-axial flow at the ends of the capillary was less than 0·1% and was neglected. Flow rates were in all cases less by a factor of about 20 than the Reynolds number for turbulent flow.

Bleakney (*Physics*, 1932, **3**, 123) proposed an empirical correction for the variation of viscosity with gas pressure. Insufficient information is available for application of systematic corrections, and for comparative reasons no allowance for any pressure variation has been made in Tables III and IV.

The Poiseuille flow equation should be corrected if the behaviour of the vapour differs appreciably from that of a perfect gas, and if this correction is not applied there will be an apparent variation with temperature of the calculated η. The most convenient way of introducing this correction is to use the equation

$$pV = n(RT + Bp)$$

in place of $pV = nRT$ in deriving the Poiseuille formula. The flow equation becomes:

$$\eta = \frac{r^4}{8L} \times \frac{273\rho}{760T} \times \frac{t}{m}\left[\frac{p_1^2 - p_2^2}{2} - \frac{B}{3}\frac{p_1^3 - p_2^3}{RT}\right]$$

Since $p_3 \sim 0$, the resultant correction can be reduced to the form:

$$\eta_{apparent} = \eta_{ideal}(1 - 2Bp/3RT)$$

where $\eta_{apparent}$ is the apparent viscosity at p, T, and η_{ideal} is the viscosity under limiting conditions of ideal gas laws. From Berthelot's equation, B is negative. By way of illustration, the numerical magnitude of the second term can be calculated at $T = 323°$ K., *viz.*: benzene = 0·0018, *cyclo*hexane = 0·0022, and *n*-hexane = 0·0023. These values refer to an arbitrary $p = 5$ cm. Hg and would be larger at lower temperatures or higher pressures (for the B values see Lambert, Roberts, Rowlinson, and Wilkinson, *Proc. Roy. Soc.*, 1949, *A*, **196**, 113).

It should be noted that any dimerisation or cluster formation has an effect on the *collision area* quite apart from the above correction to the Poiseuille equation for hydrodynamic flow.

Unfortunately, values of B are not available for all the molecules used in the present investigation, so that for comparative purposes the variation of viscosity with temperature from this cause is best left uncorrected in all the data. However, in evaluating "straight lines" for Sutherland plots anomalous data at the lowest temperatures of measurement for *iso*octane and *cyclo*octane were not included.

Results.

New results on molar volumes at the b. p. are recorded in Table I. B. p.s are used to give corresponding temperatures. New results on viscosities are conveniently summarised in the form of the parameter $\mathfrak{A} = \sqrt{MT}/\eta$, where M is the mol. wt. and T the temperature in °K. η is measured in poises.

In the simplest form of kinetic theory of momentum transfer, the molecular diameter σ is related to this parameter according to the equation:

$$\Pi\sigma^2 = \tfrac{2}{3}\sqrt{k/N\Pi} \times \sqrt{MT}/\eta = 5{\cdot}694 \times 10^{-21}\,\mathfrak{A} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where N is Avogadro's number (taken as $6{\cdot}023 \times 10^{23}$) and k is Boltzmann's constant (taken as $1{\cdot}380 \times 10^{-16}$).

These results are recorded in Table III. As will be seen below, the precision achieved in the present experiments is about the same as that in the most self-consistent previous work. Lines of closest fit were calculated by standard probability theory, using the straight-line equation (3 below). Deviations of individual mean values from these lines (Fig. 3, i—iii, p. 1969) may be compared with the scatter of individual results on which these means are based (Table III, "Precision"). The deviations accord with the experimental scatter except for one point with methyl*cyclo*pentane and one with hex-1-ene. Where necessary, further independent observations were made with different samples, but these did not remove the discrepancy. It may be that the straight-line equation assumed for purposes of computation breaks down for these molecules.

Discussion.

Coiling of n-*Paraffins in Vapour and Liquid.—Variation of* $\mathfrak{A}$ *with molecular structure.* As with other gas-kinetic parameters, the theoretical interpretation of viscosities in terms of molecular structure and modes of energy transfer has not been completely worked out for polyatomic molecules. A review up to 1934 has been given by Loeb ("Kinetic Theory of Gases," McGraw Hill, 1936). Mathematical refinements have been discussed by Chapman and Cowling ("Mathematical Theory of Non-Uniform Gases," Cambridge Univ. Press, 1939) but are not readily amenable to computation from observed viscosities. Rather elaborate computations by Hirschfelder, Bird, and Spotz (*J. Chem. Physics*, 1948, **16**, 968; *Chem. Reviews*, 1949, **44**, 205; *Trans. Amer. Soc. Mech. Eng.*, 1949, 921) are discussed below.

Although no complete theoretical treatment can at present be applied, advantage can be taken of the structural variations available within a range of homologues and isomers to establish some definite conclusions about average molecular configurations.

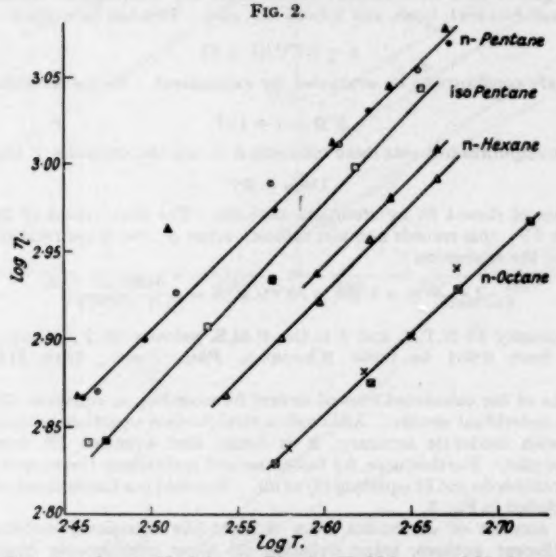
In the crudest approximation, the viscosity parameter $\mathfrak{A}$ and the molecular diameter σ effective for momentum transfer are treated as independent of temperature. Table III permits a preliminary survey of the variation of $\mathfrak{A}$ with molecular structure, in a series of closely related compounds.

So far as possible, the same temperature must be chosen for comparison. This is usually possible for isomers, but for homologues there are experimental limitations set by the vapour-pressure range in which data can conveniently be obtained. Notwithstanding these limitations, it is evident by inspection of Table III that at the same temperatures the normal paraffins have aproximately the same effective diameter as the isomeric branched paraffins. For butane the difference between the *n*- and *iso*-compounds is less than the experimental error. At longer chain length, the *n*-compounds tend to have rather higher $\mathfrak{A}$ than the branched isomers, but even for octane the difference is not more than a few units per cent. The cyclic compounds *cyclo*pentane and methyl*cyclo*pentane show a smaller $\mathfrak{A}$ than the paraffins with the same number of carbon atoms, but $\mathfrak{A}$ for *cyclo*octane resembles that for *n*-octane.

The simplest interpretation of this broad general conclusion is that in molecular collisions with similar molecules the *n*-paraffins behave as if on average their area corresponds with coiling into close-packed configurations. More detailed ratios are given in Table V below.

Molar volumes and entropies of vaporisation in relation to structure. In Table I, the molar volumes are recorded at the respective boiling points of the liquids, since these give approximately corresponding temperatures. On the average each *n*-paraffin occupies a volume which is the same within a few units per cent. as that of the isomeric branched paraffin. This again implies the broad conclusion that the average configuration of the *n*-paraffins must correspond with close-packed helices. A drift towards smaller parachors which is observed as molecular branching increases (Gibling, *J.*, 1941, 299) does not exceed 2—3% in the C_7—C_9-series. Owing to complications of molecular interference in the liquid phase, not more than a broad general comparison seems feasible at present. The smaller space requirements of cyclic molecules is again apparent and in this case is shown also by *cyclo*octane.

FIG. 2.



⊙, ⊡, △, ×, *Present work*; ●, *Nasini*; ▲, *Titani*; ⊠, *Melaven and Mach*; ■, *Bleakney* (*for refs. see Table III*).

Additional general information about the relative coiling of the flexible molecules in the liquid and the vapour may be obtained from a consideration of entropies of vaporisation (Table I, cf. Ubbelohde, *loc. cit.*). The *n*-paraffin has generally a slightly higher entropy of vaporisation than the *iso*-compound, which may imply that a rather broader distribution of configurations is assumed when the flexible *n*-paraffin molecules pass from liquid to vapour.

On this basis, the difference between isomeric *n*- and *iso*-compounds would be attributed to a change of entropy with coiling. The cyclic compounds have uniformly higher entropies of vaporisation than the paraffins with the same number of carbon atoms. This may be because for these rings in the liquid phase molecular rotation about an axis perpendicular to the symmetry axis is strongly hindered, so that the average molecular volume occupied in the liquid is smaller and the entropy of vaporisation larger than for the normal and branched-chain paraffins.

Interpretation of the temperature coefficient of viscosity. More refined information about the collision processes between polyatomic molecules can be obtained from the observed temperature variations.

Before theoretical analysis of the results is attempted, the accuracy of the temperature coefficients may be assessed. Straight lines (or shallow curves) are very generally obtained by plotting the relation,

$$\log \eta = A + s \log T \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $x > \frac{1}{3}$ (Licht and Stechhert, *J. Phys. Chem.*, 1944, **48**, 23). Such plots permit a test of concordance when the same molecule has been studied by different observers. Fig. 2 gives comparative plots for benzene, *iso*pentane, *n*-hexane, and *n*-octane. The data overlapping our present results were in most cases obtained with capillary viscometers; a rotating cylinder was used for *iso*pentane (see refs. to Table III). It will be seen from Fig. 2 that the agreement between different observers is usually within 1% for benzene; for *n*-hexane our values lie about 4% below those of Titani. For *iso*pentane our results accord with those of Bleakney within about 2·5%. For *n*-octane the concordance is generally within 1% with the results of Melaven and Mack. Except for Titani's data for *n*-hexane, the agreement is about as good as present experimental methods permit. However, the divergences make it unsafe to combine the results of more than one observer in calculating temperature coefficients, since these involve a first differential of the experimental data. The sources of the observations selected for calculation are given in Table IV. Various authors have claimed that Sutherland's equation is the most straightforward two-constant equation for the temperature coefficient of gaseous viscosity (Licht and Stechert, Loeb, and Schuil, *locc. cit.*). This can be written:

$$\eta = KT^{3/2}/(T + C) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where K and C are constants to be evaluated by experiment. In the notation of the present paper

$$K'\mathfrak{A} = 1 + C/T$$

For purposes of computation it was more convenient to use the variables T and the expression

$$T^{3/2}/\eta = \mathfrak{A}T$$

in evaluating lines of closest fit by standard methods. The best values of the constants are recorded in Table IV; this records nominal collision areas A, which are related to the constant K in equation 3 by the expression:

$$A/(1 + \epsilon) = 1{\cdot}594 \times 10^{-18}\sqrt{M}/K = \frac{0{\cdot}086\ \rho_0\bar{c}}{N\eta(1 + C/T)}$$

where ρ_0 is the density at N.T.P. and $\bar{c}$ is the R.M.S. velocity at T. Chapman's correction term ϵ ranges from 0·001 to 0·006 (Chapman, *Phil. Trans.*, 1916, **211**, 279) and is neglected.

In Fig. 3 some of the calculated lines of closest fit according to equation (3) are plotted for comparison with individual results. Although a straight-line equation represents the experimental results with moderate accuracy, it is found that equation (2) frequently gives a more nearly linear plot. Furthermore, for *iso*octane and *cyclo*octane the measured viscosities at the lowest temperatures do not fit equation (3) at all. To avoid confusion these points (Table III) have not been included in Fig. 3.

Probably on account of deviations from straight-line equations, molecular parameters calculated by different authors, using equation (3) show considerable discrepancies, even though individual values of viscosities are in good agreement. The Sutherland constant C involves extensive extrapolation and is sensitive to the precise straight line assumed.

In examining Table IV, it must be remembered that the theoretical basis for Sutherland's formula is a particular interpretation of the change of η with temperature. Sutherland's theory is that the average relative velocity of approach of the molecules increases with rise in temperature, and this lowers the apparent collision area. But if there is any other source of temperature variation of viscosity this might distort the Sutherland interpretation of the temperature coefficients. For example, if the flexible molecules are coiled, the average degree of coiling might vary with temperature (see below). Such a variation would give spurious values to the constants C and K in equation (3). Again, cyclic molecules can crumple if $n \geqslant 6$ and, particularly at higher temperatures, the relative proportions of various configurations in equilibrium can change appreciably with temperature. Furthermore, if the molecules are associated in pairs or clusters in the gas owing to van der Waals attractions this could give an abnormally large apparent collision diameter particularly at the lower temperatures.

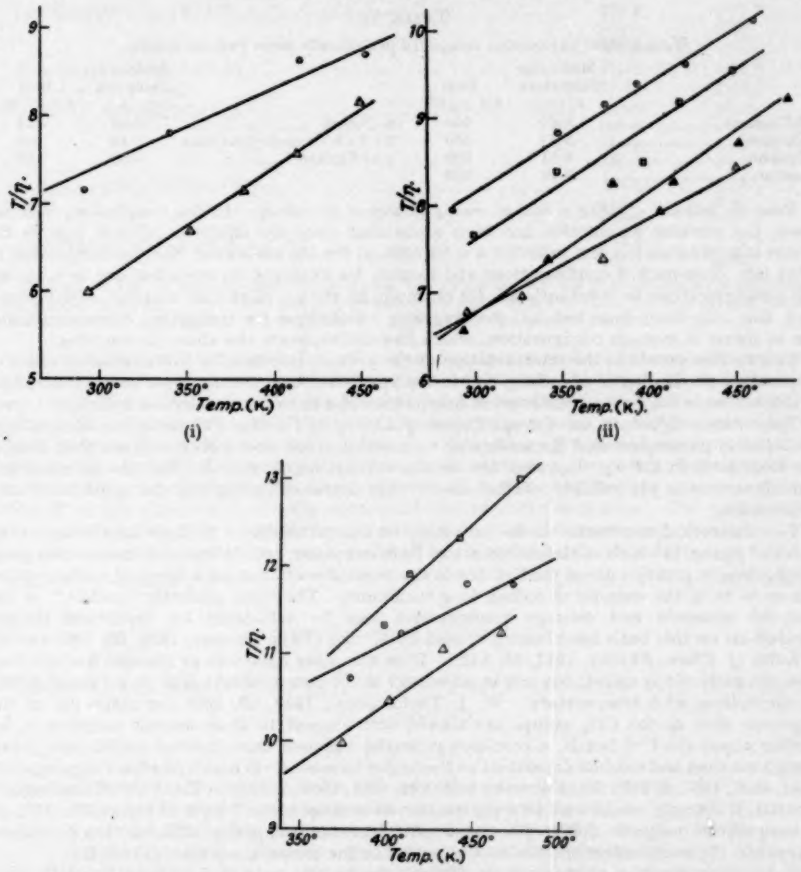
Evidence for association has been put forward on the basis of second virial coefficients (Hirschfelder, McClure, and Weeks, *J. Chem. Physics*, 1942, **10**, 201). In view of these restrictions on the Sutherland theory in the case of flexible molecules comparisons in Table IV should in the first instance be made between closely similar molecules. The Sutherland collision areas of the branched-chain paraffins are only slightly larger than those of the *n*-paraffins, thus confirming the broad conclusions from the viscosities themselves. Introduction of a double bond

at one end of *n*-hexane decreases the collision area; this is similar to the effect reported by Bleakney for pent-2-ene (*loc. cit.*).

The large apparent values of A for the cyclic compounds are anomalous and are very tentatively attributed to the fact that molecular association in the vapour is an additional source of temperature variation of viscosity. A similar anomaly has been reported for mesitylene (Everhart *et al.*, *loc. cit.*).

FIG. 3.

Sutherland plots for calculated lines of closest fit.



(i) ○, iso*Pentane*; △, cyclo*Pentane*. (ii) ○, n-*Hexane*; ⊡, *Hex*-1-*ene*; △, *Benzene*; ▲, *Methyl*-cyclo*pentane*. (iii) ⊡, cyclo*Octane*; ○, n-*Octane*; △, 2 : 2 : 4-*Trimethylpentane*.

Other computations of molecular interaction. Preliminary computations of " collision areas " were also made by the method described by Hirschfelder, Bird, and Spotz (*locc. cit.*). This method uses Lennard-Jones attraction and repulsion functions between the molecules, based on the virial coefficients. Hirschfelder, Bird, and Spotz had already reported that the *n*-hydrocarbons show large discrepancies in the force constants as evaluated from boiling-point data, compared with those evaluated from viscosities (*loc. cit.*). Graphical approximations using tables of functions calculated by these authors gave no substantially new information for the

hydrocarbons investigated by us. Results are collected in Table V. The anomaly of the cyclic compounds and the somewhat larger r_0 of the 2 : 2 : 4-trimethyl*cyclo*pentane are again apparent.

The comparisons in Table V cannot be pushed very far, since if the Taylor theory is correct (see below), a contribution to the overall temperature coefficient of viscosity would arise from the shrinking together of the coiled molecule as the temperature rises, and neither the Sutherland nor the Hirschfelder interpretation of temperature coefficient in terms of change of average molecular velocities can be fully adequate.

TABLE V.

Hirschfelder parameters computed graphically from present results.

	Molecular diameters, r_0 (A.).	Best ε/k ($\pm$25).		Molecular diameters, r_0 (A.).	Best ε/k ($\pm$25).
*cyclo*Pentane	6·69	100	*n*-Octane	6·83	450
*iso*Pentane	5·25	450	2 : 2 : 4-Trimethylpentane	7·44	300
n Hexane	6·51	300	*cyclo*Octane	8·68	150
Benzene	5·78	250			

Relation between effective collision area and degree of coiling. In the conclusions outlined above, the working assumption has been made that since the effective collision area in the vapour is approximately the same for a *n*-paraffin as for the *iso*-isomer, the *n*-paraffin must be coiled into close-packed configurations and cannot, for example, be stretched out as a zigzag. This assumption can be substantiated, for example, by the use of atomic models. Melaven and Mack (*loc. cit.*) have described a " shadowgraph " technique for computing average collision area in terms of average configuration, which likewise supports the above assumption.

Two further points in the interpretation of the present results refer to the possible effect of temperature on the degree of coiling, and to the possibility that the apparent collision area of a flexible molecule may not be the same in heteromolecular as in homomolecular collisions.

Temperature Effects in the Average Degree of Coiling of Flexible Polymethylene Molecules.— The collision parameters and the molecular volumes recorded above both indicate that flexible *n*-hydrocarbons in the C_5—C_8-range are on the average highly coiled. But the experimental methods cannot as yet indicate whether the average degree of coiling changes appreciably with temperature.

Two theoretical arguments throw some light on this possibility. If there is initially a fully stretched zigzag, in which all the carbon atoms lie in one plane, and if there is no energy change on coiling, then by rotation about the C–C bonds the molecules will assume a range of configurations such as to raise the entropy of coiling to a maximum. The most probable " radius " of the crumpled molecule and average configuration can be calculated by statistical theory. Calculations on this basis have been proposed by Eyring (*Phys. Reviews*, **1932**, **39**, 746) and by H. Kuhn (*J. Chem. Physics*, **1947**, **15**, 843). If on the other hand energy changes are involved when the molecule is coiled, the combined energy and entropy effects lead to a change of the average coiling with temperature. W. J. Taylor (*ibid.*, **1948**, **16**, 258) has made use of the suggestion that as the CH_2 groups are moved with respect to their nearest neighbours, by rotation about the C–C bonds, a repulsion potential between these nearest neighbours passes through maxima and minima dependent on the angles between C–H bonds in adjacent groups (cf. Pitzer, *ibid.*, **1937**, **5**, 469; Kistiakowsky and Stitt, *ibid.*, **1939**, **7**, 289). This " steric hindrance " potential, if correct, would lead to a contraction in average chain length of about 15—25% in the temperature range 0—200°. The consequent decrease in apparent collision area if inserted in equation (3) would affect the rise in η observed as the temperature rises (Table III).

If dA/dT is negative as required by Taylor's theory, the estimated areas in Table IV tend to be too large for the flexible molecules. This must be left for further research. Though Taylor's theory has been worked out in detail only for long chains, the behaviour predicted from it for octane and upwards appears to be in conflict with kinetic data.

By using equation (2) for interpolation of the data in Table II, it is possible to make quite precise calculations of the ratio of σ^3 for normal and branched isomers at different temperatures, according to equation (1). Some of these ratios are given as illustration in Table VI. It will be seen that the trend with temperatures of $[\sigma^3(\text{normal})/\sigma^3(iso)]$ is notably smaller than would be expected on the basis of Taylor's theory, and is, if anything, in the opposite sense. Values for the *cyclo*-compounds are also included though, for reasons stated above, the ratios may be influenced by molecular association.

TABLE VI.

Ratios of collision areas of paraffins.

	Temp. (K.).	σ_1^2/σ_2^2.
n-C_6H_{12} : $CH_3{\cdot}CH(CH_3)_2$	293·1	1·01
	373·1	1·00
	393·1	1·00
n-C_6H_{12} : $C_2H_5{\cdot}CH(CH_3)_2$	298·1	1·03
	373·1	1·02
*cyclo*Pentane : $C_2H_5{\cdot}CH(CH_3)_2$	316·2	0·83 *
	354·8	0·83
	398·1	0·87
Methyl*cyclo*pentane : n-C_6H_{14}	316·2	0·83 *
	436·5	0·87
n-C_7H_{16} : $(CH_3)_2CH{\cdot}C(CH_3)_3$	380·1	1·07
	398·1	1·07
	416·9	1·06
	436·5	1·05
n-C_8H_{18} : $(CH_3)_2CH{\cdot}CH_2{\cdot}C(CH_3)_3$	398·1	1·05
	416·9	1·05
	436·5	1·05
*cyclo*Octane : $(CH_3)_2CH{\cdot}CH_2{\cdot}C(CH_3)_3$	436·5	1·11 *
	457·1	1·13

* Equation (1) is not immediately applicable for calculating $\sigma_1^2 : \sigma_2^2$ if there is appreciable dimerisation or clustering. The dimer has a larger mol. wt. and failure to allow for this gives a ratio in which the value of σ appears too small for the more highly clustered molecules.

Homomolecular and heteromolecular collision areas. In the collision between two molecules of the same mass, to which the present data refer, possible crumpling during the collision seems likely to play a greater part than during heteromolecular impact between flexible molecules and light molecules such as hydrogen. Different apparent collision areas might be expected for the flexible hydrocarbon in the two cases. Molecules such as oxygen and nitrogen do not differ greatly in mass from the CH_2 group. Diffusion studies of the C_{16}—C_{18}-polymethylene molecules in air (Bradley and Shellard, *Proc. Roy. Soc.*, 1949, *A*, **198**, 239) lead to conclusions about coiling in the gas phase which roughly correspond with present conclusions. The special case of collisions with hydrogen is being further investigated in view of the interesting catalytic rôle of hydrogen in certain hydrocarbon reactions (Small and Ubbelohde, *J.*, 1950, 723).

QUEEN'S UNIVERSITY, BELFAST. [*Received, February 26th*, 1951.]

---

440. *Cinnolines. Part XXVII.* The Preparation and Nitration of Cinnoline.*

By J. S. MORLEY.

Nitration of cinnoline in concentrated sulphuric acid gives 8-nitrocinnoline and an isomeric mononitrocinnoline in approximately equal proportion; the latter differs from 6-nitro- and 7-nitro-cinnoline and is regarded as the 5-nitro-compound. Cinnoline is best prepared by decarboxylation of cinnoline-4-carboxylic acid in benzophenone during which 4 : 4′-dicinnolyl is formed as a minor product. Catalytic reduction of 4-chloro- or 4 : 7-dichloro-cinnoline gives only a little cinnoline or 7-chlorocinnoline; in the former case the main product is 4 : 4′-dicinnolyl.

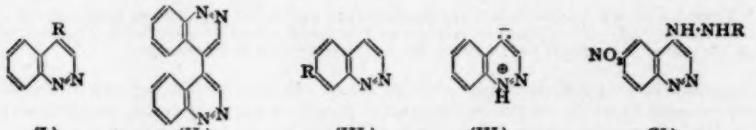
As one extension of the previous work on the comparative chemistry of simple heterocyclic systems (Simpson *et al.*, *J.*, 1948, 360; 1949, 1014, 1354, 1356; 1950, 1104), it is planned to study the qualitative nitration of the bicyclic bases under comparable conditions. In this respect, the nitration of quinoline and *iso*quinoline is well known and that of quinazoline has recently been described (Elderfield *et al.*, *J. Org. Chem.*, 1947, **12**, 405; Schofield and Swain,

* Part XXVI, *J.*, 1950, 392.

J., 1949, 1367). The present paper describes preliminary work on the preparation and nitration of cinnoline (I; R = H).

Cinnoline was first prepared by reduction of 4-chlorocinnoline (I; R = Cl) with iron and 15% sulphuric acid to 1 : 2-dihydrocinnoline, which gave cinnoline when oxidised with mercuric oxide (Busch and Rast, *Ber.*, 1897, **30**, 521). In contrast, catalytic hydrogenation of (I; R = Cl) with palladium on calcium carbonate, under conditions which convert 4-chloroquinazoline into 3 : 4-dihydroquinazoline in almost quantitative yield (Elderfield *et al.*, *loc. cit.*, and confirmed), gave only a trace of cinnoline, the main product being a compound, m. p. 232°, analysis of which suggested 4 : 4′-dicinnolyl (II) (see below). Likewise, catalytic reduction of 4 : 7-dichlorocinnoline gave only a little 7-chlorocinnoline (III; R = Cl), after ferricyanide oxidation.

An alternative route to cinnoline (Jacobs *et al.*, *J. Amer. Chem. Soc.*, 1946, **68**, 1310) is decarboxylation of cinnoline-4-carboxylic acid (I; R = CO_2H), prepared from 4-methylcinnoline (I; R = Me) *via* 4-styrylcinnoline (I; R = CH:CHPh). The conditions and high yields for these reactions were found to be readily reproducible, and since 4-methylcinnoline itself is now prepared in excellent yield from methyl anthranilate (Jacobs *et al.*, *loc. cit.*, and confirmed), this is to be preferred as a preparative route to cinnoline. The final decarboxylation of (I; R = CO_2H) gives, in addition to cinnoline, a small amount (5·6% average yield) of the compound, m. p. 232°, prepared by catalytic reduction of 4-chlorocinnoline; this can therefore be regarded as 4 : 4′-dicinnolyl (II).



(I.) (II.) (III.) (IV.) (V.)

The production of (II) by decarboxylation of (I; R = CO_2H) in benzophenone is of interest in that Brown, Hammick, and Thewlis (*Nature*, 1948, **162**, 73) report that, under similar conditions, the related quinoline-4-carboxylic acid gives 7—10% of diphenyl-4-quinolylcarbinol, and Mislow (*J. Amer. Chem. Soc.*, 1947, **69**, 2559) has shown that *iso*nicotinic acid gives 3·5% of diphenyl-4-pyridylcarbinol. If, as seems probable from analogy with the work of Hammick *et al.* (*J.*, 1937, 1724; 1939, 809; 1949, 173, 659; *Nature*, *loc. cit.*), the decarboxylation of (I; R = CO_2H) occurs *via* the protonised cinnolyl anion (IV), then the reason for the formation of (II) in preference to a carbinol such as is formed in the quinoline and pyridine series, may well lie in changes governing the competition of the intermediate anion, on the one hand, and the decarboxylated base or benzophenone on the other, within the three heterocyclic series. The increased reactivity of the 4-position in the cinnoline nucleus towards anionoid reagents in comparison with the quinoline nucleus has already been commented on (Keneford, Morley, Simpson, and Wright, *J.*, 1950, 1104).

Nitration of cinnoline in concentrated sulphuric acid gave a mixture of two mononitrocinnolines in good yield, which were readily separated by fractional crystallisation from benzene and sublimation. That least soluble in benzene was identical with a specimen of 8-nitrocinnoline, m. p. 132·5—133·5°, kindly supplied by Dr. K. Schofield (Alford and Schofield, unpublished work). The other nitrocinnoline, m. p. 152—153°, markedly depressed the m. p. of both 6-nitro- (see below) and 7-nitro-cinnoline (III; R = NO_2), m. p. 153—154° (Dr. Schofield); since nitration in the hetero-ring is unlikely in the conditions used, the compound is regarded as 5-nitrocinnoline. Both nitrocinnolines from the nitration were extremely sensitive to warm dilute sodium hydroxide solution, but they were stable to hot 4N-ammonia solution and to mineral acids. 8-Nitrocinnoline was mostly unchanged after being refluxed for a short time with phosphorus pentachloride and oxychloride; reductive acetylation gave 8-acetamidocinnoline in poor yield as the sole identifiable product. 5(?)-Nitrocinnoline gave no useful product on treatment with stannous chloride, iron and acetic acid, hydrogen and palladium or Adams's catalyst, and alkaline sodium dithionite.

4-Chloro-6-nitrocinnoline reacted readily with hydrazine and toluene-*p*-sulphonhydrazide in chloroform giving 4-hydrazino-6-nitrocinnoline (V; R = H) and 6-nitro-4-toluene-*p*-sulphonylhydrazinocinnoline (V; R = *p*-Me·C_6H_4·SO_2). Neither of these hydrazines could be oxidised successfully by aqueous copper sulphate, nor could a crystalline product be obtained by their

decomposition with alkalis. However, 4-hydrazino-6-nitrocinnoline gave a hydrazone with acetone, which was readily converted by aqueous copper sulphate oxidation into 6-nitrocinnoline, m. p. 205—206°. This differed from either of the two nitrocinnolines prepared by direct nitration of cinnoline.

Earlier work (Keneford, Morley, Simpson, and Wright, *loc. cit.*) has shown that in reactivity 4-substituted cinnolines occupy a position intermediate between those of quinolines and quinazolines. It is clear, however, that so far as nitration is concerned, cinnoline resembles quinoline, which gives 5- and 8-nitroquinoline in about equal proportions, and is quite distinct from quinazoline, from which only the 6-nitro-compound (56%) has been isolated (Elderfield *et al.*, *loc. cit.*; Schofield and Swain, *loc. cit.*). There are, however, many puzzling features in the nitration of nitrogenous heterocyclic compounds (cf. Schofield, *Quart. Reviews*, 1950, **4**, 382), and the reaction as it applies to benzodiazines cannot be usefully discussed further until more facts are available.

Experimental.

Cinnoline.—The yields of this base and its intermediates in the preparation from methyl anthranilate were in close agreement with those obtained by Jacobs *et al.* (*loc. cit.*): 2-*o*-aminophenylpropene (86%, methylmagnesium iodide being used); 4-methylcinnoline (90%); 4-styrylcinnoline (theoretical yield on 1-mole scale; m. p. 120—123°; a digestion of the dried, crude hydrochloride with benzene was advantageous); cinnoline-4-carboxylic acid (81% on 0·4-mole scale, an efficient glass stirrer being used); cinnoline (72·5%). Cinnoline hydrochloride monohydrate (long, brittle, pale-green needles from ethanol–ether) melted between 82° and 137° to a clear, pale-green melt, which darkened and decomposed at 205°. Cinnoline, b. p. 114°/0·35 mm., solidified during the distillation; the solid had m. p. 40—41° and slowly liquefied to a green liquid on being set aside in air. There is, however, no appreciable decomposition of the base since cinnoline picrate was formed in quantitative yield from liquid which had been exposed to the atmosphere for two months.

4 : 4′-*Dicinnolyl.*—Cinnoline-4-carboxylic acid was decarboxylated in 5-g. batches by the procedure described by Jacobs *et al.* (*loc. cit.*). The combined reaction mixture from four such runs was dissolved in ether (720 ml.) and extracted with N-hydrochloric acid (400 ml.; in three portions). The acid extracts were then washed once with ether, cooled in an ice-bath, saturated with potassium carbonate, and extracted with ether. 4 : 4′-*Dicinnolyl*, m. p. 233—234°, was obtained by (*a*) evaporation of the ethereal extracts (charcoal) to 300 ml. (0·24 g.; average of two runs), and (*b*) filtration of the remaining aqueous suspension from the extraction, followed by digestion of the residue with water (0·51 g.; average of two runs). After further removal of the ether from the ethereal extracts (corresponding to eight 5-g. decarboxylations), cinnoline (21·7 g.) distilled at 114°/0·35 mm. An additional crop of 4 : 4′-dicinnolyl (0·75 g.; m. p. 204—206°) was obtained by digestion of the residue from this distillation with water (75 ml.); the aqueous digest contained cinnoline, isolated as the picrate (1·22 g.), m. p. 195—196°. Pure 4 : 4′-dicinnolyl (total yield 7·5% based on cinnoline-4-carboxylic acid) formed long, soft, pale-yellow needles, m. p. 237—238°, from aqueous acetic acid (Found: C, 74·2; H, 4·0; N, 21·7. $C_{16}H_{10}N_4$ requires C, 74·4; H, 3·9; N, 21·7%).

Catalytic Reduction of 4-*Chlorocinnoline.*—The chloro-compound (2·0 g.) in methanol (100 ml.) was shaken with palladium hydroxide on calcium carbonate catalyst [10 g., prepared by Busch and Stöve's procedure (*Ber.*, 1916, **49**, 1063)] at room temperature and 4—5 atmospheres' pressure of hydrogen during 15 minutes. Evaporation under reduced pressure of the filtered, deep-red solution gave a sticky, brown solid, which was digested with hot water (40 ml.) and filtered in the cold. The residue (0·46 g.), m. p. 195—197° (decomp.), was insoluble in 2N-sodium hydroxide solution (20 ml.) and gave small, brittle, golden prisms, m. p. 231—232° (mixed m. p. 235—237°), of 4 : 4′-dicinnolyl (0·15 g.) after two recrystallisations from ethanol (7 parts) (Found: C, 73·6; H, 4·2; N, 21·3%). The original aqueous digest, after concentration in a vacuum, was treated with 4N-sodium carbonate solution (15 ml.), the solution filtered from calcium carbonate (0·45 g.), and the filtrate saturated with potassium carbonate. Ether extraction gave a brown oil, which yielded cinnoline picrate (90 mg.), m. p. and mixed m. p. 190—191°, after treatment with alcoholic picric acid.

Catalytic Reduction of 4 : 7-*Dichlorocinnoline.*—The chloro-compound (2·0 g.), hydrogenated exactly as above, gave a residue, after evaporation of the filtered solution, which was dissolved in water (50 ml.). Treatment with 33% potassium hydroxide solution (15 ml.), followed by a solution of potassium ferricyanide (6·5 g.) in hot water (50 ml.) and addition of 33% potassium hydroxide solution (100 ml.) after 10 minutes, gave 7-*chlorocinnoline* (0·29 g.; isolated by ether extraction), which formed fine needles, m. p. 92—93°, from water (in which it was appreciably soluble) (Found: C, 57·9; H, 3·1; N, 17·2. $C_8H_5N_2Cl$ requires C, 58·4; H, 3·05; N, 17·0%).

Nitration of Cinnoline.—Powdered cinnoline (10 g.) was added with stirring during ½ hour to a mixture of concentrated sulphuric acid (50 ml.) and fuming nitric acid (50 ml., *d* 1·50) at −5°. The temperature was then allowed to rise to 20° during 1 hour, the clear, yellow-green solution was then poured on ice (1 kg.), and the mixture partly neutralised with 20% aqueous sodium hydroxide at 0°, and finally made alkaline with solid potassium carbonate. Extraction of the resulting suspension with benzene and concentration of the combined, dried (anhydrous $CuSO_4$) extracts to 50 ml., gave a yellow solid *X* (6·04 g.), m. p. 111—118°, on cooling, and a solid *Y* (4·1 g.), m. p. 117—125°, on further evaporation and addition of light petroleum (b. p. 60—80°).

Recrystallisation of solid *X* from benzene (80 ml.) gave long, yellow needles (3·77 g., 28%), m. p. 135—136°, of 8-*nitrocinnoline* (mother liquors *Z*), which after further recrystallisations melted constantly at 136—138°. There was no depression in m. p. on admixture with genuine 8-nitrocinnoline, m. p. 132·5—133·5°. After adsorption on alumina (Peter Spence, Grade H), and elution with benzene, the nitrocinnoline was recovered almost quantitatively and the m. p. had dropped to 133—134° (m. p. and mixed m. p.), unchanged after recrystallisation (Found: C, 55·1; H, 2·85; N, 23·8. $C_8H_5O_2N_3$ requires C, 54·9; H, 2·9; N, 24·0%).

The mother liquors *Z*, after evaporation to 10 ml., gave a solid (1·84 g.), m. p. 110—114°, which after sublimation at 80°/0·05 mm. and rejection of the first (50 mg.) and later crops, gave a combined sublimate (1·34 g.), m. p. 140—142°, of 5(?)-*nitrocinnoline*. This was likewise obtained from solid *Y* by sublimation at 90°/9·05 mm. (3·06 g.; m. p. of various sublimates, 141—144° to 144—146°). The total yield was 4·4 g. (33%). Repeated sublimation and recrystallisation from absolute ethanol gave mustard-yellow needles of pure 5(?)-nitrocinnoline, m. p. 151—152° (Found: C, 54·9; H, 2·7; N, 24·0%). A mixture with 8-nitrocinnoline had m. p. 111—113°, with 6-nitrocinnoline m. p. 125—126°, and with 7-nitrocinnoline m. p. 113—118°.

Both nitrocinnolines were easily soluble in cold chloroform and acetone, and in hot water, ethanol, benzene and ethyl acetate; 5(?)-nitrocinnoline was, however, very appreciably more soluble in cold benzene and in cold ethyl acetate. 5(?)-Nitrocinnoline, in particular, darkened on storage. Each was recovered unchanged after being refluxed for 1 hour with 2N- or concentrated hydrochloric acid or with 4N-ammonia solution.

Decomposition of the Nitrocinnolines by Sodium Hydroxide Solution.—(*a*) To a solution of 8-nitrocinnoline (100 mg.) in hot water (8 ml.) was added 2N-sodium hydroxide solution (1 ml.); there was an immediate colour change from yellow through deep red to a deep olive-green. Acidification of the cold solution with dilute hydrochloric acid gave a dark amorphous solid (50 mg.), m. p. >300°, soluble in cold alkalis and reprecipitated on acidification, but insoluble in most organic solvents. (*b*) 5(?)-Nitrocinnoline likewise gave an amorphous solid (70 mg.), m. p. >300°.

8-*Acetamidocinnoline*.—8-Nitrocinnoline (1 g.), acetic anhydride (20 ml.), and anhydrous sodium acetate (0·4 g.) were treated at 90—95° with zinc dust (1·5 g.) added during 10 minutes; after a further ½ hour at 90—95°, the suspension was warmed with water (120 ml.), the hot solution filtered (charcoal), and the filtrate neutralised at 0° with 4N-ammonia solution. Extraction with ether (750 ml. in all), and evaporation of the dried (K_2CO_3) extracts, gave a sticky solid residue (0·41 g.), which formed dense prisms, m. p. 174—175°, of 8-*acetamidocinnoline* (0·11 g.) from benzene (5 ml.); after further recrystallisation from benzene–light petroleum (b. p. 60—80°) this melted at 177—178° (Found: C, 64·25; H, 4·5; N, 22·6. $C_{10}H_9ON_3$ requires C, 64·15; H, 4·8; N, 22·45%). The *picrate* formed yellow needles, m. p. 238—239° (decomp.), from aqueous ethanol (Found: C, 45·9; H, 3·15; N, 20·1. $C_{10}H_9ON_3,C_6H_3O_7N_3$ requires C, 46·15; H, 2·9; N, 20·2%). A tan-coloured granular solid (0·29 g.), m. p. 240—242° (decomp.), was obtained from the ammoniacal aqueous phase, from the above ether extraction, by saturation with solid potassium carbonate and extraction with chloroform.

4-*Hydrazino*-6-*nitrocinnoline*.—(*a*) When freshly prepared 4-chloro-6-nitrocinnoline (5 g.), dissolved in cold dry chloroform (100 ml.), was treated with hydrazine hydrate (5 ml.; 90%) and enough absolute ethanol (up to 30 ml.) to give a homogeneous solution, maroon-coloured crystals of the crude hydrazine (5·4 g.), decomposing sharply at 233°, separated after 1 hour, and a further crop (0·3 g.), was obtained by keeping the solution overnight. A solution in N/2-hydrochloric acid was basified with ammonia solution, and a maroon solid, m. p. >330°, was obtained. A suspension of this (0·35 g.) in hot ethanol (50 ml.) was treated with concentrated hydrochloric acid (1—2 ml.) and filtered; golden-coloured needles (0·22 g.) of the *hydrochloride* separated on cooling, which decomposed at 215° (Found: C, 40·3; H, 3·6; N, 27·9; Cl, 14·7. $C_8H_7O_2N_5,HCl$ requires C, 39·8; H, 3·35; N, 29·0; Cl, 14·7%).

(*b*) The crude hydrazine (2·2 g.), m. p. >330°, was likewise obtained from the chloro-compound (2 g.), hydrazine hydrate (2 ml.; 90%), and ethanol (100 ml.); the suspension was shaken for 5 minutes, stored overnight, and filtered.

6-*Nitro*-4-iso*propylidenehydrazinocinnoline* (*Acetone* 6-*Nitro*-4-*cinnolylhydrazone*).—The above crude hydrazine (0·5 g.) was refluxed with acetone (50 ml.) for 10 minutes; dilution with water (50 ml.) gave the crude *hydrazone* (0·35 g.), m. p. 176—177°, which formed orange, hair-like needles (or, occasionally, maroon needles), m. p. 179—180°, from aqueous acetone (Found: C, 53·6; H, 4·35; N, 25·65. $C_{11}H_{11}O_2N$ requires C, 53·7; H, 4·55; N, 28·7%).

6-*Nitrocinnoline*.—Acetone 6-nitro-4-cinnolylhydrazone (0·2 g.), water (2 ml.), and 10% aqueous copper sulphate solution (4 ml.) were refluxed for ½ hour; filtration of the hot solution and cooling of the filtrate gave a yellow solid (0·12 g.), which formed yellow needles, m. p. 205—206°, of 6-*nitrocinnoline* after recrystallisation from ethanol (Found: C, 54·7; H, 2·95; N, 24·2, 23·8. $C_8H_5O_2N_3$ requires C, 54·9; H, 2·9; N, 24·0%).

6-*Nitro*-4-*toluene*-p-*sulphonylhydrazinocinnoline*.—Solutions of toluene-*p*-sulphonhydrazide (1·6 g.) and 4-chloro-6-nitrocinnoline (2 g.; freshly prepared) in cold chloroform (each 100 ml.) were mixed and set aside at room temperature for 2 days. After decantation of the supernatant liquid, the dark-red, sticky tar, which had separated, was washed with chloroform and digested with acetone (50 ml.) giving a brown, granular solid (2·02 g.), m. p. 187—189°, which gave the *hydrazine* (1·55 g.) after crystallisation from aqueous acetic acid; the pure compound formed glittering, orange-red needles, m. p. 212—213° (decomp.), from aqueous acetone (Found: C, 49·8; H, 3·4; N, 19·4. $C_{15}H_{13}O_4N_5S$ requires C, 50·1; H, 3·65; N, 19·5%). It had only weak basic properties, formed a deep green solution in dilute sodium hydroxide solution, and was very sparingly soluble in hot ethanol and in hot acetic acid, and insoluble in ether, benzene, and chloroform. When a solution of the hydrazine (0·4 g.) in 0·5N-sodium hydroxide solution (25 ml.) was kept at 90° for 3 hours, nitrogen was evolved but no benzene-soluble material was left; acidification gave a flocculent, dirty-brown, amorphous precipitate, m. p. >300°. The

hydrazine was likewise not decomposed smoothly by sodium carbonate–ethylene glycol (cf. Albert and Royer, *J.*, 1949, 1148). It was recovered unchanged after being refluxed for a short period with 3% aqueous copper sulphate solution.

The author gratefully acknowledges the advice and encouragement he has received from Dr. J. C. E. Simpson.

WARRINGTON YORKE DEPARTMENT OF CHEMOTHERAPY,
LIVERPOOL SCHOOL OF TROPICAL MEDICINE.
MEDICAL RESEARCH COUNCIL, GROUP FOR RESEARCH IN CHEMOTHERAPY,
DEPARTMENT OF ORGANIC CHEMISTRY,
THE UNIVERSITY, MANCHESTER.

[*Received, March 7th*, 1951.]

---

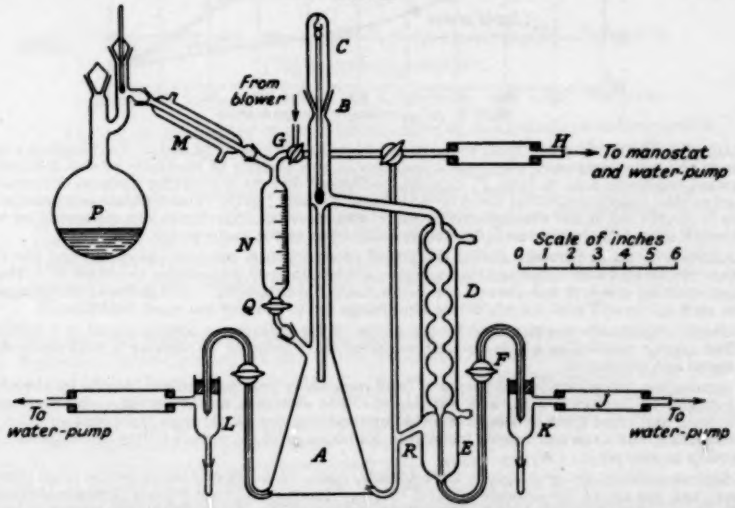
441. *The Liquid–Vapour Equilibrium as a Function of Temperature for the System Arsenic Trichloride–Germanium Tetrachloride.*

By F. SEBBA.

The liquid–vapour equilibrium for the system arsenic trichloride–germanium tetrachloride has been investigated. The curve shows no azeotropes, and therefore the two components can be separated by fractional distillation.

ARSENIC is an almost invariable contaminant of naturally occurring germanium, and its removal by purely chemical means is a laborious process. However, at some stage in its extraction it is usual to distil germanium as the volatile tetrachloride from a fairly concentrated hydrochloric acid solution. Under these conditions much of the arsenic remains in the residue, but it has been a matter of experience that, although the boiling point of germanium tetrachloride is 83·1° and that of arsenious chloride is 130·0°, some arsenic trichloride invariably distils with the germanium tetrachloride. The vapour–liquid equilibrium for the binary mixture arsenic trichloride–germanium tetrachloride has now been investigated.

FIG. 1.



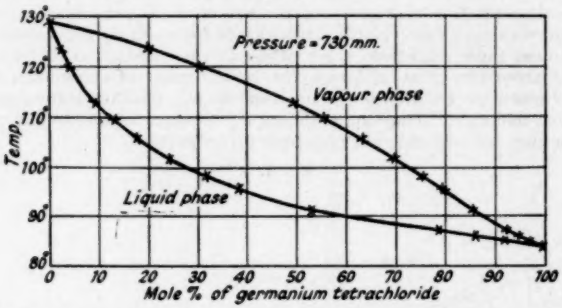
The method used was basically that of the Othmer still (Othmer, *Ind. Eng. Chem.*, 1943, **35**, 614). Some modification was necessary for the following reasons: (*a*) because of the comparative rarity and high cost of germanium care had to be taken that no germanium tetrachloride was lost; (*b*) as germanium tetrachloride is readily hydrolysed by atmospheric moisture, all access to the outside atmosphere had to be controlled; (*c*) in view of the dangerously poisonous nature of arsenic trichloride, this precaution reduced hazards from that source; and (*d*) a further difficulty arose because of the solvent effect of both these covalent compounds on tap-greases. Even silicone greases, though better than hydrocarbon

tap-greases, failed to prevent leakage completely, and mercury seals were unsuitable as arsenic trichloride readily attacks mercury. The final form of the apparatus which overcame most of these difficulties is shown in Fig. 1.

A was basically the Othmer still, made from a 750-ml. Erlenmeyer flask; the neck *B* was longer than would normally be necessary, because a sensitive thermometer with a ground-glass fitting was not available. As arsenic trichloride attacks rubber, a rubber stopper could not be used; the thermometer, therefore, was suspended completely inside the apparatus from a glass hook inside stopper *C*, platinum wire being used. *D* was a condenser, enabling the distillate representative of the vapour phase to be collected in *E*, with overflow running back into *A* through the tube *R*, which was inserted into the boiler *A* by means of a narrow inner-sealed tube. In the original Othmer design, the distillate was sampled through a tap directly below *E*, but because of the solvent effect of the liquids on the tap-grease, this arrangement was modified by having a capillary tube of swan-neck design with a tap *F* above the level of the liquid in *E*. In this way, direct contact of the liquid with the tap, except when sampling, and thus loss of liquid due to gravity leakage, was avoided. When required for sampling, a small positive pressure in the apparatus was produced with dried (phosphoric oxide) air from a blower circuit, introduced through tap *G*, and the liquid pushed over. After sampling, the liquid was returned to *E*, by slight suction through the circuit *H*. This connected the apparatus to a water-pump through a phosphoric oxide trap.

In order to sample the liquid from *E*, without its exposure to moist atmosphere, the arrangement at *K* was used. *K* was connected to the water-pump by way of tube *J*, which contained solid sodium hydroxide to collect any germanium tetrachloride vapours, and a tube which contained phosphoric oxide. At the bottom of *K* was a small ground-glass joint to which a tared weighing-bulb, fitted with a ground-glass joint, could be attached. A sample could be pushed into the weighing bulb by operating the blower and opening *F*. The bulb with its sample was then quickly stoppered. *K* was closed by attaching a second small bulb at the bottom and any excess of liquid pumped off through the sodium hydroxide trap, the water-pump being used.

FIG. 2.



For sampling the liquid phase in *A*, there was an identical arrangement at *L*. To introduce a sample of either of the pure components into the apparatus in the absence of moisture, it was distilled from concentrated sulphuric acid in flask *P*, through condenser *M* into a metering cylinder *N*, which was graduated so that known quantities could be introduced through tap *Q*. The distillation proceeded more smoothly if carried out below atmospheric pressure, and therefore this circuit was connected by way of tap *G* through sodium hydroxide and phosphoric oxide traps to the water-pump.

To maintain constant pressure during the period of equilibrium between the liquid and the vapour phase, the Othmer still was connected through *P* to a manostat and manometer to circuit *H*. The most convenient working pressure was about 2 cm. below normal atmospheric. It was found advantageous to cover the neck of the still with loosely fitting aluminium foil to prevent too much heat loss.

The arsenic trichloride was prepared by the action of dry chlorine on arsenic metal in a combustion tube. The arsenic trichloride which distilled was freed from chlorine by shaking it with finely divided arsenic metal and redistilled.

The germanium tetrachloride was prepared from reasonably pure germanium dioxide by the addition of concentrated hydrochloric acid, and distillation. The distillate was collected under concentrated sulphuric acid, and freed from hydrogen chloride by bubbling dry air through it for half an hour. The only contaminant was a trace of arsenic trichloride, and because of the nature of this investigation, it was not necessary to remove it.

The flask containing the germanium tetrachloride, under concentrated sulphuric acid was placed in position *P*, and 100 ml. of the chloride distilled into the metering cylinder *N*, at a pressure of about 500 mm. The germanium chloride was then run into the boiler *A*. Flask *P* was interchanged with the flask containing the arsenic trichloride, and small quantities, as required, usually in 10-ml. portions, were distilled into *N*, again under reduced pressure, and run into the boiler *A*. The mixture in *A* was then boiled gently, and the distillate collected in *E*, the overflow returning to boiler *A*. The distillation was carried out at a fixed pressure of 730 mm., adjustment being made on the manostat, before an experiment, to allow for changes in the barometric pressure. At frequent intervals a few bubbles of dry air were allowed to leak into *E* and *A* through the swan-neck tubes, to ensure mixing of the small amount of liquid trapped in the bends.

When the temperature had remained steady for some 20 minutes, it was recorded, the distillation was stopped, and after cooling and a preliminary flushing of the swan-neck tubes with the liquid in *A* and *E*, samples were collected at *L* and *K* as previously described. After being weighed, the stoppered weighing-tubes were opened under dilute sodium hydroxide solution. The solution obtained was neutralised with sodium hydrogen carbonate, and the arsenic titrated with standard iodine solution. The germanium chloride content was obtained by difference.

After the determination with the 50–50 mixture, the boiler *A* was cleaned, and the procedure repeated starting with pure arsenic trichloride in the boiler and adding small quantities of germanium tetrachloride.

Fig. 2 shows the results obtained, plotted as molar percentage composition of the vapour and the liquid phase against temperature. The curve showed that these two components give no azeotropes, and it should, therefore, be comparatively simple to separate the two components by use of an efficient fractionating column. This was confirmed by fractionally distilling a mixture of arsenious trichloride and germanium tetrachloride through an 18-in. column filled with Fenske glass helices. In these circumstances the germanium tetrachloride distillate showed no sign of arsenic contamination by macroanalytical tests.

This conclusion offers no evidence that the same conditions will apply when the distillation is carried out in the presence of the extra components, hydrogen chloride and water. On the contrary, experience indicates that the distillates from such a mixture are complex, the germanium tetrachloride distilling in two stages, some at about 80° and the rest at about 105°. The reasons for this are unknown and therefore this system merits fuller investigation.

It is suggested, however, that in order to obtain germanium tetrachloride free from arsenic trichloride by a distillation process, it should first be distilled from hydrochloric acid and collected under sulphuric acid, whereby it is dried. After being freed from hydrogen chloride by bubbling air through it, the germanium chloride should be distilled through an efficient fractionating column; this should give a product sufficiently free from arsenic contamination for most chemical purposes, though for use in rectifying valves further refinement may be necessary.

The author expresses his thanks to Professor W. Pugh for the interest shown and the facilities extended.

UNIVERSITY OF CAPE TOWN. [*Received, March 7th,* 1951.]

---

442. *The Probable Existence of Geometrically Isomeric Diazocarboxyamides.*

By H. C. FREEMAN, R. J. W. LE FÈVRE, and I. R. WILSON.

The dipole moment of the one known form of benzenediazocarboxyamide is 3·9 D., a value which is consistent with a *trans*-configuration about the azo-group. After exposure to sunlight, solutions in benzene show signs of a slight increase of solute polarity; parallel experiments with ethanol solutions give spectrophotometric indications similar to those previously observed with diazocyanides and various other N : N-containing molecules. The fact that geometrical isomers of the structure, R·N:N·CO·NH_2, have not so far been actually isolated cannot therefore be taken as contrary to the views of Hantzsch.

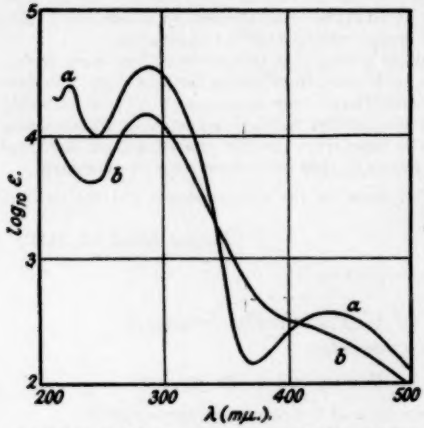
DURING the relevant researches of Hantzsch, beginning about half a century ago (see Saunders, "The Aromatic Diazo-Compounds and Their Technical Applications," 2nd edn., Arnold and Co., London, 1948, Chap. XI, for references) isomers of types generalisable as R–N:N–X were successfully isolated only when X was O–Metal (diazoates), CN (diazocyanides), or SO_2·O–Metal (diazosulphonates). All other diazo-derivatives seemed to occur as single forms, a fact which, while not opposed, was unhelpful to Hantzsch's stereochemical ideas concerning the –N:N– group. The discovery of a second and more polar variety of azobenzene (Hartley, *J.*, 1938, 633; Hartley and Le Fèvre, *J.*, 1939, 531) and of a similar multiplicity of other azoaryl compounds (Cook and Jones, *J.*, 1939, 1309) has therefore been a particularly important step in the modern development of the subject (cf. Hodgson, *J.*, 1948, 1097; Le Fèvre and Souter, *J.*, 1949, 1595), while recently Le Fèvre and Worth (*J.*, 1951, 1814) have reported indications that 2 : 2′-azopyridine exists as more than one form. Accordingly a re-examination is now in hand of certain cases, notably diazocarboxyamides, diazoamino-compounds, diazo-ethers, and diazo-sulphones, where Hantzsch found no isomerism.

This paper records experiments showing that aryldiazocarboxyamides undergo changes by the action of light which parallel in essential respects those previously described for a number of diazocyanides and diazosulphonates, for azobenzene, and for 2 : 2′-azopyridine (cf. Calderbank, Le Fèvre, and Northcott, *Chem. and Ind.*, 1948, 158; Le Fèvre, Northcott, and Wilson, *ibid.*, p. 732; Freeman and Le Fèvre, *J.*, 1950, 415; Le Fèvre and Worth, *loc. cit.*).

Three diazocarboxyamides, R·N:N·CO·NH_2, have been prepared with R = Ph, *p*-Br·C_6H_4, and *p*-NO_2·C_6H_4. All were sparingly soluble in non-polar solvents, the first-named being least so. By using concentrations up to saturation (which seemed to be about 0·45% at 25°) in benzene, we have estimated the dipole moment of C_6H_5·N:N·CO·NH_2 as 3·9 D., when measurements were made in the absence of daylight. One hour's exposure to the sun caused slight increases in the solute polarity. Interpretation of these results might have been assisted by corresponding data for the *p*-Br·C_6H_4-compound but unfortunately the maximum w_1 achieved at 30° was less than 0·08%.

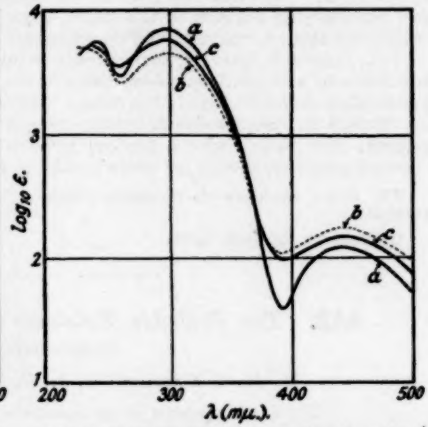
Two comments seem justifiable: (*a*) In a *trans*-configuration of R·N:N·CO·NH_2 the two C ⟶ N moments associated with the azo-group should approximately cancel, leaving a molecular resultant of the order of that for benzamide; such is in fact the case, the two

FIG. 1.



(*a*) Ph·N_2·CO·NH_2. (*b*) *p*-NO_2·C_6H_4·N_2·CO·NH_2.

FIG. 2.



p-Br·C_6H_4·N_2·CO·NH_2: (*a*) *before irradiation*; (*b*) *after irradiation*; (*c*) *solution from* (*b*) *after* 24 *hours in the dark.*

recorded values for the last-named substance being $\mu = 3{\cdot}6$ (Devoto, *Gazzetta*, 1933, **63**, 129) and 3·8 (Davis, Bridge, and Svirbely, *J. Amer. Chem. Soc.*, 1943, **65**, 857). (*b*) For a *cis*-configuration of R·N:N·CO·NH_2 there can be no certainty concerning the direction of action of the component vector due to the CO·NH_2; it will most probably not lie along the N_2–amide link, and could easily be roughly at right angles to a "*cis*-azo"-component of *ca.* 3 D. (*i.e.*, $\mu_{cis\text{-azobenzene}}$). The molecular resultant to be expected would then be obviously about 5 D.

Clearer evidence of the type sought has been obtained with dilute ($0{\cdot}5 \times 10^{-4}$ M.) solutions of the three diazocarbonamides in 96% ethyl alcohol. When made up and kept in the dark these gave absorption spectra as in Figs. 1 and 2 (curve *a*). It was found that the light source in the Beckman spectrophotometer used had no influence on the results, but exposure of the filled cells to the unfiltered radiation from a mercury-discharge lamp caused changes in the intensities of absorption at the absorption peaks. These changes became gradually reversed when irradiated solutions were kept in the dark although ultimately their initial absorption features were only partly reproduced. Fig. 2 (curve *c*) illustrates the degree of this recovery. As a check on the experimental technique, samples from a bulk solution of benzenediazocarboxyamide stored in an opaque flask were examined at intervals during four days and gave transmission readings which varied by only small amounts, such as could be attributed to slight solvent loss during cell filling and emptying, etc., which were much less than the alterations following illumination by the mercury lamp.

It will be noted that the general forms of the curves in Fig. 1 resemble those of the related diazocyanides (cf. Le Fèvre and Wilson, *J.*, 1949, 1106), so that, by analogy, the modifications of intensity by irradiation now observed are in the directions to be expected if, by the action of light, a fraction of the *trans*-molecules are (reversibly) transformed into their *cis*-isomers.

These details are summarised in Tables I and II. Hantzsch and Lifschitz (*Ber.*, 1912, **45**, 3011) recorded a spectrum of benzenediazocarboxyamide between the "Schwingungzahlen" 2600 and 4300. One absorption maximum is shown at about 282 mμ., with indications that others exist in the regions outside the limits 235—400 mμ.; in general outline therefore these earlier results appear to resemble ours.

TABLE I.

Spectra of diazocyanides and diazocarboxyamides.

	Diazocyanides (stable forms).		Diazocarboxyamides.	
Aryl group.	$\lambda_{max.}$ (mμ.).	$\log_{10} \varepsilon_{max.}$	$\lambda_{max.}$ (mμ.).	$\log_{10} \varepsilon_{max.}$
Ph	—	—	434	2·57
	—	—	286	4·54
	—	—	223	4·39
p-Br·C_6H_4	425	2·77	440	2·09
	341	4·50	300	3·87
	238	4·09	245	3·77
p-NO_2·C_6H_4	443	2·38	420	2·4 *
	308	4·22	283	4·16
	277	3·94 *		

* Point of inflexion.

Irradiation of saturated alcoholic solutions of benzenediazocarboxyamide or of its *p*-bromo-derivative for 4 hours produced no evident decomposition or visible colour change. Recovery of the solute either by cooling to −30° or by precipitation with water gave samples, melting at 115° and 177°, which were apparently identical with our initial preparations. Such homogeneity in the solid state could be caused by association, between the amide groupings, on the pattern of formulæ (I*a* and *b*) shown by Chaplin and Hunter (*J.*, 1937, 1116) since clearly steric requirements would best be satisfied when all the $-N{:}N-$ units have the *trans*-configuration.

TABLE II.

Effects of irradiation on $\log_{10}\varepsilon$ *at stated wave-lengths.*

	Diazocyanides.		Diazocarboxyamides.		
Aryl group.	$\lambda_{max.}$ (mμ.).	$\log_{10} \varepsilon_{spm.}$ minus $\log_{10} \varepsilon_{unirr.}$	Irradiation period (hrs.).	λ (mμ.).	Change in $\log_{10} \varepsilon$.
Ph	—	—	4	287·5	+0·04
	—	—	4	220	+0·03
p-Br·C_6H_4	341	−0·6	2·4	300	−0·12
	425	+0·3	2·4	440	+0·07

Our experience with benzenediazocarboxyamide appears to differ from that of Hantzsch and Schultze (*Ber.*, 1895, **28**, 2073), who abandoned the examination of this substance because of its instability. Their specimens were obtained from the oily benzenediazocyanide, which we have previously found (*J.*, 1949, **333**) to be hard to purify and difficult to keep. For the present work we have obtained our material *via* the oxidation of 1-phenylsemicarbazide—a route which leads to highly crystalline products.

EXPERIMENTAL.

Solutes.—Benzenediazocarboxyamide was obtained from phenylsemicarbazide (Thiele, *Ber.*, 1895, **28**, 2599); it formed red needles, m. p. 114°, from benzene. In connection with possible hydrogen-bond formation it is noteworthy that from water this material can separate as a hydrate, m. p. 84° (Thiele, *loc. cit.*). The *p*-bromo- and *p*-nitro-benzenediazocarboxyamides were easily produced by refluxing the corresponding diazocyanides with water (Hantzsch and Schultze, *Ber.*, 1895, **28**, 666, and *loc. cit.*); recrystallised from alcohol they had m. p. 177° and 183° respectively. We confirm that as solutions in alcohol these substances do not couple with alcoholic or alkaline β-naphthol either before or after irradiation by ultra-violet light (cf. Hantzsch and Schultze, *loc. cit.*; Hodgson and Marsden, *J.*, 1944, 395).

Dipole Moments and Related Observations.—The apparatus, symbols and methods used are those described in *J.*, 1949, 333. Solutions could not be prepared with the cold solvent. The solutes were accordingly weighed into tared brown bottles, benzene was added, the mixtures were boiled until dissolution was complete, and the final weighings (bottle and solution) were made on cooling. Table III presents our measurements on benzenediazocarboxyamide and its *p*-bromo-derivative. Owing to the

low solubility and consequent unavoidable experimental errors, the moment quoted for the second solute cannot be regarded as more than an estimate of order of magnitude.

TABLE III.

Benzenediazocarboxyamide in benzene at 25°.

10^5w_2.	ε_{12}.	d_{12}.	$a\varepsilon_2$.	βd_2.
0	2·2725	0·87378	—	—
2040	2·2955	0·87425	11·3	$0{\cdot}23_0$
2708	2·3043	0·87419	11·7	$0{\cdot}15_1$
3016	2·3054	0·87423	10·9	$0{\cdot}14_9$
3157	2·3083	0·87461	11·3	$0{\cdot}26_2$
4215	2·3170	0·87451	10·6	$0{\cdot}17_3$
		Mean	11·2	$0{\cdot}19_3$

Whence, with $[R_L]_D$ calc. = 48·7 c.c., and M_1 = 149·15, we find $_TP$ = 353·9 c.c., $_OP$ = 305·2 c.c., and μ = 3·86 D.

p-Bromobenzenediazocarboxyamide in benzene at 30°.

10^5w_1.	ε_{12}.	d_{12}.	$a\varepsilon_2$.	βd_2.
0	2·2628	0·86718	—	—
376	2·2660	0·86746	8·5	$0{\cdot}75_5$
401	—	0·86746	—	$0{\cdot}60_4$
455	2·2670	0·86742	9·2	0·53
465	2·2663	—	7·5	—
720	—	0·86761	—	0·60
732	—	0·86748	—	0·41
		Mean	8·4	0·58

Whence, with $[R_L]_D$ calc. = 59·4 c.c., and M_1 = 228·1, we find $_TP$ = 390 c.c., $_OP$ = 331 c.c., and μ = about 4 D.

The changes in dielectric constant (all measured at 25°) produced by illumination (sunlight) of benzene solutions of benzenediazocarboxyamide are shown by their $a\varepsilon_2$ values in Table IV, where line (i) gives $a\varepsilon_2$ for each original solution, and lines (ii) and (iii) the same property first after one hour in sunlight and then after 24 hours in darkness.

TABLE IV.

10^5w_1	2040	2708	3016	3157	4125
$a\varepsilon_2$ (i)	11·3	11·7	10·9	11·3	10·6
$a\varepsilon_2$ (ii)	12·7	12·8	11·8	12·4	11·2
$a\varepsilon_2$ (iii)	11·2	12·1	17·1 *	13·4 *	— *

* These solutions were cloudy when measured for the third time, showing that crystallisation had commenced.

The results for the first and second solutions were not inconsistent with a reversible photochemical change. With all five solutions there seemed to be an increase in the polarity of the solute. The two cases not marred by crystallisation show that we have not wrongly drawn this conclusion from an irreversible concentration change caused by evaporation of this solvent.

The authors gratefully acknowledge financial assistance from the Commonwealth Science Fund.

UNIVERSITY OF SYDNEY, N.S.W., AUSTRALIA. [*Received, March 7th*, 1951.]

---

443. *The Determination of Oxiran-oxygen, with Special Reference to its Application to the Study of Autoxidation.*

By GEORGE KING.

A quantitative study of the absorption of hydrogen chloride from organic solvents by certain 1 : 2-epoxides and olefinic ketones has been made. A simple method of determining epoxides based on this principle, without strictly anhydrous conditions, has been further developed and critically examined. It has been shown that the presence of a carbonyl group may interfere with the quantitative absorption of hydrogen chloride by an epoxide, and α-olefinic ketones may also absorb hydrogen chloride to a variable extent.

The application of the method to the investigation of the autoxidation of oleic acid has been exemplified. In this connexion, the absorption of ultra-violet light in the region of λ 220 mμ. has been used to estimate the concentration of κ- and η-keto-oleic (10- and 7-ketoheptadec-8-ene-1-carboxylic) acids and hence to apply suitable corrections to the oxiran-oxygen values.

trans-11-Ketoheptadec-9-ene-1-carboxylic acid has been further studied, and its ultra-violet absorption spectrum recorded.

IT has generally been assumed that the absorption of hydrogen chloride from organic solvents by 1 : 2-epoxides is more or less quantitative (Nicolet and Poulter, *J. Amer. Chem. Soc.*, 1930, **52**, 1186; Swern *et al.*, *Analyt. Chem.*, 1947, **19**, 414). In a preliminary communication

(*Nature*, 1949, **164**, 706) the author described a convenient method of determining epoxides, based on the absorption of hydrogen chloride from a solution of hydrochloric acid in dioxan during ten minutes. The results obtained with simple epoxides, such as oleic and elaidic acid oxides, were nearly quantitative and compared favourably with those obtained by earlier methods, involving strictly anhydrous conditions and a much longer time of contact. It was subsequently shown, however, that the presence of neighbouring reactive groups, such as carbonyl, as in λ-ketoelaidic acid oxide, may interfere with the absorption; further, that certain unsaturated ketones, more especially those of the type R·CO·CH:CHR′, also absorb hydrogen chloride (King, *J.*, 1950, 2897), a property which assumes particular importance when the method is applied to the autoxidation products of unsaturated fatty acids. These defects appear to be inherent in all methods based on the absorption of hydrogen chloride from organic solvents, whether anhydrous or not. Ross's method (*J.*, 1950, 2257), based on the development of alkalinity when an epoxide is boiled with an aqueous-acetone solution of sodium thiosulphate, is inapplicable to the determination of long-chain epoxides of the type under investigation.

Table I records the oxiran-oxygen values found for a variety of 1 : 2-epoxides, and the absorption of hydrogen chloride by certain olefinic ketones is given in Table II. Of the epoxides studied, λ-ketoelaidic acid oxide is exceptional in absorbing only 72% of the theoretical quantity

TABLE I.

	Oxiran-oxygen (%).		
	HCl–dioxan method.	Method of Swern *et al.*	Theory.
Oleic acid oxide	5·19	5·18	5·36
Elaidic acid oxide	5·17	5·19	5·36
Ethyl oleate oxide	4·66	4·62	4·90
Ricinelaidic acid oxide	4·92	5·10	5·09
λ-Ketoelaidic acid oxide	3·68	3·58	5·12
Epichlorohydrin	16·76	—	17·30
Butadiene monoxide	21·60	21·50	22·8

TABLE II.

	Mols. of HCl absorbed per mol. of substance.	
	HCl–dioxan method.	Method of Swern *et al.*
λ-Keto-oleic acid	0·10	0·13
λ-Ketoelaidic acid	0·01	—
κλ-Diketo-oleic acid	0·15	0·14
Mesityl oxide	0·22	0·65
	0·49 (2 hours)	
	0·60 (3 hours)	
trans-11-Ketoheptadec-9-ene-1-carboxylic acid	0·90	0·93
Benzylideneacetone	Nil	—

of hydrogen chloride, a result which may be attributed to the influence of the carbonyl group. The absorption by unsaturated ketones under these conditions is very variable and is sometimes mainly dependent on the time of contact (see, *e.g.*, mesityl oxide, Table II). The α-olefinic ketone *trans*-11-ketoheptadec-9-ene-1-carboxylic acid (I) absorbs hydrogen chloride rapidly and almost quantitatively. This compound is closely analogous to the structurally isomeric κ- (II) and η-keto-oleic acids (III) and the corresponding ketoelaidic acids, which appear in significant amounts during the autoxidation of oleic and elaidic acids at 50—60° (Ellis, *Biochem. J.*, 1950, **46**, 129; *J.*, 1950, 9).

$$\underset{\text{(I.)}}{R\cdot CO\cdot CH{:}CH\cdot[CH_2]_2\cdot R'} \qquad \underset{\text{(II.)}}{R\cdot CH_2\cdot CO\cdot CH{:}CH\cdot CH_2R'}$$

$$\underset{\text{(III.)}}{R\cdot[CH_2]_3\cdot CH{:}CH\cdot CO\cdot R'} \qquad \underset{\text{(IV.)}}{R\cdot CO\cdot CH_2\cdot CH{:}CH\cdot CH_2R'}$$

$$(R = CH_3\cdot[CH_2]_5;\ R' = [CH_2]_4\cdot CO_2H.)$$

Although (II) and (III) have not yet been isolated, they are known to give rise on alkaline hydrolysis to the volatile nonan-2-one and nonaldehyde, respectively, whereby their concentrations in autoxidised oils may be estimated with reasonable accuracy. By analogy with (I), it is highly probable that these keto-acids absorb some 90% of the theoretical amount of hydrogen chloride required per double bond under the conditions used for the determination of oxiran-oxygen, and the latter values for the total autoxidation products of oleic or elaidic acid must be corrected accordingly.

The acid (I) has now been studied in further detail. Its ultra-violet absorption spectrum (Fig. 1) exhibits a band of high intensity ($\epsilon_{max.}$ 16,000) at 224 mμ. and a weak band ($\epsilon_{max.}$ 53) at 317 mμ., thus closely resembling that of κλ-diketo-oleic (*cis*-10 : 11-diketoheptadec-8-ene-1-carboxylic) acid (King, *J.*, *loc. cit.*). A value of $\epsilon_{max.}$ 16,000 in the region of 220 mμ. appears to be consistently associated with the group ·CO·CH:CH·, and it may be assumed that the spectra of the analogous acids (II) and (III) have bands of the same intensity in this region. The absorption spectrum of oleic acid, autoxidised at 70—80° in the presence of a cobalt catalyst, also exhibits a peak at *ca.* 220 mμ., and the increase in the extinction at this wave-length, which runs closely parallel to the amount of volatile oil obtainable by alkaline hydrolysis, affords an alternative, and probably more accurate, basis for the determination of the total κ- and η-keto-acid content.

FIG. 1.

Absorption spectrum of trans-11-*ketoheptadec-9-ene-1-carboxylic acid.*

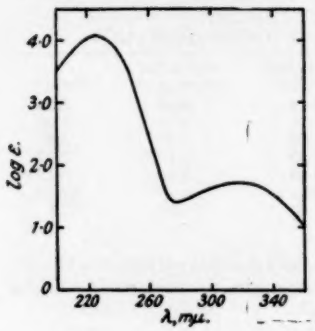
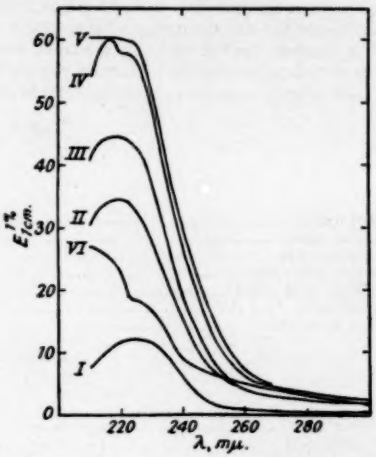


FIG. 2.



I. Original oleic acid. *IV. After* 9 *hours' autoxiation.*
II. After 3 *hours' autoxidation.* *V.* ,, 12 ,,
III. ,, 6 ,, *VI.* ,, 31 ,,

A typical example of the application of the spectrophotometric method to the assessment of olefinic keto-acid formation during the catalytic autoxidation of oleic acid and the influence of such acids on the observed oxiran-oxygen values is summarised in Table III and Fig. 2. Oxygen was bubbled through oleic acid containing 0·5% of cobalt at 77—78°. The total concentration of keto-acids (II and III) was calculated from the increase in the absorption at 224 mμ. on the assumption that the pure acids have $\epsilon_{max.}$ 16,000 at or very near this wave-length, and it was further assumed that they absorb 90% of the theoretical amount of hydrogen chloride, equivalent to an apparent oxiran-value of 4·85%. The final verification of these assumptions necessarily awaits the isolation of (II) and (III) in a pure state; nevertheless, remarkably good

TABLE III.

Autoxidation at 77—78° *of oleic acid containing* 0·5% *of cobalt.*

Time (hours)	0	3	6	9	12	31
Equiv. wt.	282	287	284	266	246	197
I Val. (Wijs, ¼ hour)	85	70	56	39	24	6
Active oxygen (Lea), %	Trace	0·03	0·03	0·04	0·04	0·05
Apparent oxiran-O, %	0·18	0·71	1·03	1·45	1·63	0·77
$E^{1\%}_{1\ cm.}$ cm. at λ 224 mμ.	12	34	44	58	60	19
κ- and η-Keto-oleic acids, %	—	4·2	6·1	8·7	9·1	1·3
Oxiran-O (corr.), %	—	0·51	0·73	1·03	1·19	0·71
Elaidic acid oxide, %	—	9·5	13·6	19·2	22·2	13·3
Volatile hydrolysis products,* %, found	—	1·6	2·9	3·9	3·7	0·6
Volatile hydrolysis products,* %, calc.	—	2·0	2·9	4·2	4·4	0·6

* Nonan-2-one, nonanal, and nonanoic acid.

correspondence was observed between the total steam-volatile hydrolysis products, consisting of nonan-2-one, nonaldehyde, and a little nonanoic acid arising from atmospheric oxidation, and the calculated amounts. The progressive increase in the keto-acid concentration up to a maximum of some 9% after 12 hours' oxidation was also closely paralleled by the intensity of the purple colour which developed on treatment of the autoxidised oil with 3 : 5-dinitrobenzoic acid in ethanolic sodium hydroxide, but was insufficient to cause a perceptible peak in the ultra-violet light absorption at 317 mμ. The maximum content of epoxide in terms of elaidic acid oxide was 22%, which accords well with the 16—20% actually isolated by Ellis (*Biochem. J.*, 1936, **30**, 753) after similar autoxidations.

The marked fall in the amounts of keto-acid and epoxide on prolonged oxidation was presumably caused by chain scission at the double bond, and to ester formation resulting from union of the epoxide with itself or with acid cleavage products (Ellis, *Biochem. J.*, 1950, **46**, 129). The concentration of peroxides was low throughout. No κλ-diketo-oleic acid (King, *J., loc. cit.*) could be detected among the products, and it may be inferred that little or no λ-keto-oleic acid is formed under these conditions, since it undergoes autoxidation to the former very rapidly.

It may be remarked that the absorption of ultra-violet light below 240 mμ. by ordinary commercial samples of " oleic acid " is not usually due to the presence of keto-acids. Such impure samples commonly have $E^{1\%}_{1\,cm.}$ values of about 25 at 220—225 mμ., yet contain no measurable amount of keto-oleic acids; the dinitrobenzoic acid test is virtually negative and no volatile oil is obtained when the acid is boiled with dilute alkali.

The absorption of hydrogen bromide from dioxan or ether solution by (I) affords almost exclusively 9-bromo-11-ketoheptadecane-1-carboxylic acid, m. p. 70·5°, which also results from the addition of hydrogen bromide to λ-keto-oleic (or elaidic) acid (IV) and from which (I) is readily regenerated by the action of cold aqueous alkali. Similarly, (I) combines with hydrogen chloride to form an adduct, m. p. 70°, which, by analogy with the bromo-compound, is probably 9-chloro-11-ketoheptadecane-1-carboxylic acid. Oxidation of (I) with alkaline permanganate at 100° gives *n*-heptanoic and sebacic acids.

Experimental.

Determination of Oxiran-oxygen.—The method used was essentially that already described (*Nature, loc. cit.*), but greater accuracy was achieved by using double quantities, *i.e.*, 0·2 g. of epoxide-containing material and 20 ml. of the dioxan–hydrochloric acid reagent, followed after 10—15 minutes by 20 ml. of neutral ethanol. The epoxide was weighed out in a conical flask of 150-ml. capacity, carrying a ground-glass stopper, and the reagent was delivered from a burette to avoid inhaling the vapour unnecessarily. In most cases the method of Swern *et al.* (*loc. cit.*) was also used for comparison.

Autoxidation of Oleic Acid.—Oleic acid was purified by the method of Brown and Shinowara (*J. Amer. Chem. Soc.*, 1937, **59**, 6) and had $E^{1\%}_{1\,cm.}$ 12 at 224 mμ. Oxygen was bubbled at the rate of 30 ml. per minute by way of a sintered-glass filter-stick through the acid (16 ml.) at 77—78°, finely powdered cobalt hydroxide (0·5% as Co) being added as a catalyst. Samples (2 ml.) of the oil were withdrawn at intervals for analysis. After 9 hours or more the cooled product deposited some unidentified crystalline material.

κ- and γ-Keto-oleic Acids (II and III).—The total concentration of these acids was calculated from the increase in the value of $E^{1\%}_{1\,cm.}$ at 224 mμ. The pure keto-acids being assumed to have $E^{1\%}_{1\,cm.}$ 540 ($\varepsilon_{max.}$ 16,000) at this wave-length, their percentage concentration is given by $(E^{1\%}_{1\,cm.} - 12)/5{\cdot}28$. All absorption spectra were examined in ethanol with a Unicam Model S.P. 500 Spectrophotometer.

Correction of Oxiran-oxygen Values.—By analogy with (I), the keto-acids (II) and (III) were assumed to absorb 0·9 mol. of hydrogen chloride under the above conditions, corresponding to an apparent oxiran-oxygen value of 4·85%. Thus, of the total oxiran-oxygen value of 1·63% observed after 12 hours' autoxidation (Table III), 0·44% was contributed by the keto-acids (9·1%), leaving a corrected value of 1·19%, equivalent to a content of 22·2% of elaidic acid oxide.

Volatile Hydrolysis Products.—The autoxidised oil (*ca.* 1 g.) in 0·1N-sodium hydroxide (100 ml.) was very slowly distilled, and the insoluble steam-volatile products were quantitatively collected in a special trap (Ellis, *Biochem. J., loc. cit.*). It was confirmed that this volatile oil consisted largely of nonan-2-one (semicarbazone, m. p. 117—118° not depressed by an authentic specimen) with a small proportion of nonanal (crude 2 : 4-dinitrophenylhydrazone, m. p. 94° raised to 96—97° by an authentic specimen) and some 11—12% of nonanoic acid arising from atmospheric oxidation of the latter. It gave a weak Schiff's test and the proportion of nonanal was insufficient to give any crystalline deposit with dimedone in 50% ethanol.

trans-11-*Ketoheptadec-9-ene-1-carboxylic Acid* (I).—This acid was prepared by the following modification of Ellis's method (*J., loc. cit.*). λ-Ketoelaidic acid (8·4 g.), m. p. 72·5°, in dioxan (250 ml.) was shaken with concentrated hydrobromic acid (20 ml.; *d* 1·7) at intervals during 1 hour. The diluted and cooled solution deposited 9-bromo-11-ketoheptadecane-1-carboxylic acid, which crystallised from *n*-hexane in needles (9·6 g.), m. p. 70·5° (Found: C, 57·6; H, 8·9; Br, 21·0. Calc. for $C_{18}H_{33}O_3Br$: C, 57·3; H, 8·8; Br, 21·2%). The product was dissolved in 0·25N-sodium hydroxide (450 ml.) and

kept for 1 hour at room temperature. Acidification with acetic acid then afforded (I), which crystallised from acetic acid in thin hexagonal plates (6·1 g.), m. p. 50·5°, freely soluble in warm light petroleum, but sparingly soluble at 0° [Found: C, 72·9; H, 10·9%; equiv., 296; I.V. (Wijs, 45 minutes), 83·4. Calc. for $C_{18}H_{32}O_3$: C, 72·9; H, 10·9%; equiv., 296; I.V., 86]. The *semicarbazone* separated from ethanol in hexagonal tablets or prisms, m. p. 141·5° (Found: C, 64·7; H, 9·7; N, 12·0. $C_{19}H_{35}O_3N_3$ requires C, 64·5; H, 10·0; N, 11·9%).

The acid (I) absorbed 90% of the theoretical amount of hydrogen chloride required for 1 double bond under the above conditions, equivalent to an apparent oxiran-oxygen value of 4·85%. It gave a deep purple colour with 3 : 5-dinitrobenzoic acid in ethanolic sodium hydroxide, by which as little as 10 μg. could be detected. Its absorption spectrum in ethanol had $\varepsilon_{max.}$ 16,000 at 224 mμ. and a feeble maximum $\varepsilon_{max.}$ 53 at 317 mμ. Hydrolysis of the acid with 0·05N-sodium hydroxide afforded a 38% yield (theory, 43%) of octan-2-one (2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 68·5°).

Oxidation of trans-11-*Ketoheptadec-9-ene-1-carboxylic Acid* (I).—The acid (0·75 g.) was dissolved in 0·5% aqueous sodium hydroxide (20 ml.) and heated with potassium permanganate (1·7 g.) in water (20 ml.) at 100° for 10 minutes. The cooled solution was acidified with concentrated hydrochloric acid, saturated aqueous sodium metabisulphite (1 ml.) was added, and the whole diluted to about 120 ml. with water. Distillation afforded *n*-heptanoic acid (0·24 g.) (Found: equiv., 128. Calc. for $C_7H_{14}O_2$: equiv., 130), whose zinc salt crystallised from ethanol in rectangular plates, m. p. and mixed m. p. 136°. The residual solution, cooled at 0°, deposited sebacic acid (0·37 g.), which was dissolved in ether and reprecipitated by addition of 2 volumes of *n*-hexane; it then crystallised from water in thick rhombic and hexagonal plates, m. p. and mixed m. p. 132° (Found: equiv., 102. Calc. for $C_{10}H_{18}O_4$: equiv., 101).

9-*Chloro*-11-*ketoheptadecane*-1-*carboxylic Acid*.—The acid (I) (0·54 g.) in dioxan (25 ml.) was shaken with concentrated hydrochloric acid (1 ml.) in a stoppered flask and left for 1 hour. The diluted and cooled solution deposited 9-*chloro*-11-*ketoheptadecane*-1-*carboxylic acid* (0·58 g.), which crystallised from *n*-hexane in needles, m. p. 70° (Found: C, 64·7; H, 9·9; Cl, 10·5%; equiv., 327. $C_{18}H_{33}O_3Cl$ requires C, 64·9; H, 10·0; Cl, 10·7%; equiv., 333). This compound has already been prepared from λ-keto-oleic acid by Dr. G. W. Ellis (private communication).

Other Materials.—λ-Keto-oleic acid, m. p. 40°, and λ-ketoelaidic acid, m. p. 73° (Ellis, *loc. cit.*); oleic acid oxide, m. p. 59·5° (King, *J.*, 1942, 390); elaidic acid oxide, m. p. 55·5°, and ethyl oleate oxide, m. p. 21° (King, *J.*, 1948, 1820); ricinelaidic acid oxide, m. p. 65—66°, λ-ketoelaidic acid oxide, m. p. 84°, and κλ-diketo-oleic acid (King, *J.*, 1950, 2897); mesityl oxide, b. p. 130—132°, purified by washing with aqueous alkali and fractionation.

The author is indebted to Imperial Chemical Industries Limited for a sample of butadiene monoxide.

St. Mary's Hospital Medical School, London, W.2. [*Received, April 9th*, 1951.]

---

444. *The Kinetics of the Autoxidation of* n-*Decanal. Part I. The Mechanism of Reaction.*

By H. R. Cooper and H. W. Melville.

The autoxidation of *n*-decanal to per-acid has been investigated kinetically by means of measurements of oxygen absorption in an automatically controlled manostat. Bäckström showed that this was a radical chain reaction which could be initiated by ultra-violet light, but the detailed mechanism remained uncertain. As usual with radical processes of long chain length, reliable results require care to ensure that the solution of oxygen in the aldehyde does not become the rate-controlling factor. To reduce the proportion of the thermal reaction, experiments were conducted at 5°. Evidence is presented which indicates that: (1) The mechanisms of the thermal and photo-processes are identical apart from the mode of initiation. (2) Chain propagation occurs by the usual cycle: $R\cdot + O_2 \longrightarrow RO_2\cdot$; $RO_2\cdot + RH \longrightarrow ROOH + R\cdot$. (3) In the pressure region ½—1 atm., termination takes place wholly by the mutual interaction of the peroxidic radicals. (4) Thermal initiation involves direct attack by oxygen on the aldehyde molecules, and photo-initiation direct dissociation of the aldehyde into radicals.

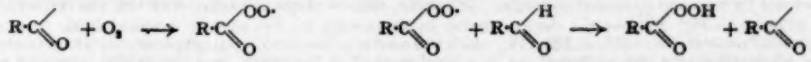
During an investigation of "negative catalysis," reported during 1926—1934, Bäckström showed that autoxidation of aldehydes in the liquid phase proceeded by a peroxidic mechanism, the initial product being a per-acid. From the large quantum yield (of the order 10^4) observed when the process was carried out under the influence of ultra-violet radiation, and from the drastic reduction in the rate of autoxidation brought about by the addition of small quantities of substances such as α- and β-naphthol, he deduced that the per-acid formation, whether brought about thermally or photochemically, was a chain reaction; in this way the foundation

of the theory of thermal chain reactions was laid. Subsequent reaction between the per-acid and further aldehyde by a non-chain mechanism gave rise to the final product of autoxidation, the carboxylic acid, and this secondary process was found to be almost insensitive to the action of ultra-violet light, *i.e.* :

(*a*) Aldehyde + Oxygen ⟶ Per-acid

(*b*) Aldehyde + Per-acid ⟶ Carboxylic acid

Bäckström concluded that the chain carriers involved in stage (*a*) were of a free-radical nature and suggested that the propagation steps were of the form :



He found experimental evidence to support the view that substances which inhibited the autoxidation acted by removing the peroxidic radicals from the system.

Bowen and Tietz's results (*J.*, 1930, 234) on the gas-phase photochemical autoxidation of acetaldehyde indicated that the reaction rate was of the form :

$$\text{Rate} \quad \propto I^{\frac{1}{2}}[\text{R·CHO}]^{1}[\text{O}_2]^{0}$$

where I represents the intensity of the absorbed light, and this suggested that the chains were being terminated by mutual destruction of the radical chain-carriers.

It appeared, therefore, that the first stage in the autoxidation of aldehydes bore a formal similarity to that shown recently to hold for olefinic hydrocarbons by the investigations of the British Rubber Producers' Research Association (*Proc. Roy. Soc.*, 1946, *A*, **186**, 218 *et seq.*). This similarity has been emphasised by the results reported in the present paper. A complete kinetic examination of the thermal and photochemical autoxidation of *n*-decanal in the liquid phase has enabled a detailed mechanism to be evolved for both processes and, by the use of modern experimental techniques (see Part II), the velocity constants of some of the individual reaction steps involved have been measured. The knowledge of these quantities and of similar results from work on related systems can lead to generalisations about the reactivity of the radicals concerned.

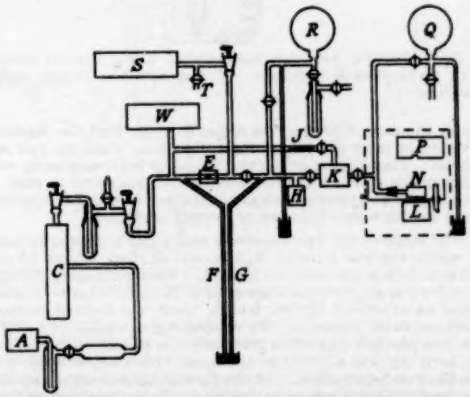
Experimental.

General Outline of Apparatus.—As pure oxygen was used, it was necessary to be able to evacuate the reaction system. Pressures of 10^{-4} mm. or less could be achieved by a two-stage mercury diffusion pump backed by a Speedivac rotary oil-pump.

The general lay-out of apparatus is shown in Fig. 1.

Fig. 1.

General outline of apparatus.



A, Oil pump. C, Mercury diffusion pump. E, Vacustat. H, Mercury dropper. J, Capillary. K, Manostat. L, Electromagnetic stirrer. N, Silica reaction vessel. P, Mercury lamp. Q, Nitrogen bulb. R, Oxygen bulb. S, Distillation system. W, Aldehyde reservoir and sampling devices. T, Nitrogen inlet.

The storage bulbs for oxygen and oxygen-free nitrogen were periodically filled from cylinders of the appropriate gases, but the oxygen was introduced through a liquid-air trap to ensure removal of condensable impurities. The actual oxygen pressure in the reaction system was measured by the difference in the mercury levels in tubes *F* and *G*.

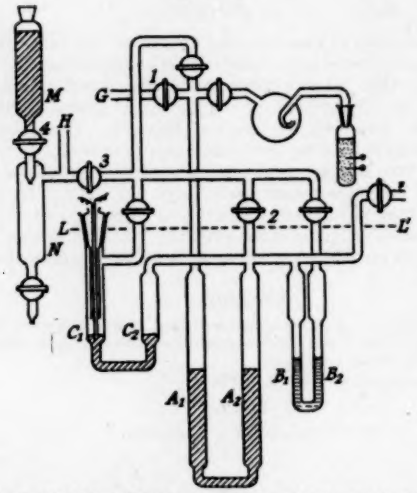
Both the manostat and the reaction vessel were immersed in water-thermostats, controlled by A.C. Thyratron relays operated in conjunction with mercury–toluene regulators of the usual type. The low temperatures required were obtained by circulating water, cooled by a refrigerating unit, through the copper tank containing the reaction vessel. The temperature in the copper tank was regulated, within $\pm 0{\cdot}01°$, by running the refrigerating unit all the time and operating, in opposition, a heating lamp through the Thyratron circuit and the mercury–toluene regulator.

Except where likely to come into close contact with the aldehyde, Apiezon Grease M was used as a lubricant for taps and ground-glass joints. Otherwise, silicone grease thickened with talc was employed.

Manostat.—Fig. 2 shows the device, similar in dimensions to, but slightly modified from, that of Bolland (*Proc. Roy. Soc.*, 1946, *A*, **188**, 218), which was used to follow the oxygen uptake at constant pressure. The whole apparatus was immersed, up to a level marked in the figure, in a thermostat regulated at $25{\cdot}00° \pm 0{\cdot}01°$. The thermionic relay circuit controlling the manostat was that employed by Bolland. Current for the electrolytic cell was obtained from the D.C. mains through a potentiometer device, for

FIG. 2.

Manostat.



A_1A_2, Oxygen burette. B_1B_2, Dibutyl phthalate manometer. C_1C_2, Contact manometer. F, Connection to reaction vessel. G, Connection to capillary. H, Connection to oxygen supply and vacuum. LL', Water level in thermostat.

it must be possible to vary the rate of production of gas in order that the manostat may function with maximum efficiency at different rates of oxygen absorption (*i.e.*, when the cell is "on" and "off" for approximately equal times). The volume of oxygen taken up was measured, within 0·02 mm., on the limb A_2 of the gas burette beside which was fixed a steel rule graduated in mm. Since the tubing was found to be of even bore, there is no appreciable loss of accuracy in using a constant factor (1·12 c.c./cm.) to convert distances along the limb into volumes of oxygen absorbed.

Although only the initial stage of the oxidation was examined, preliminary experiments showed that the amount of oxygen which the gas burette A_1A_2 could deliver—about 18 c.c.—was rather small. Somtimes, it was desirable to follow the reaction further. Since increasing the diameter of the limbs in the gas burette would involve less accurate measurement of the oxygen uptake, and since the depth of the thermostat tank prevented an extension of their length, there was devised instead a method of refilling A_1A_2 at an approximately constant pressure. By connecting a capillary (*J* in Fig. 1) between A_1 and the main vacuum line it was possible to reduce gradually the pressure in A_1 through tap 1. Further, with taps 2 and 3 open, mercury was allowed at the same time to flow from *M* to *N*, so reducing the volume of the oxygen in the reaction system. If the flow of mercury was carefully reguated by tap 4, the reduction of pressure and the contraction of volume could be balanced so that the oxygen pressure remained almost constant. Any deviation from the original pressure was indicated by the dibutyl phthalate manometer. The time taken for this operation was less than 3 minutes and, by noting the rate of oxygen uptake before and after refilling, the volume of oxygen absorbed by the sample in the interim could be estimated if required.

Reaction Vessel.—The silica reaction vessel used for this investigation had plane-parallel circular faces 2 cm. apart and 6 cm. in diameter. This type of vessel minimises the dispersing effects of the glass on the incident light, but its chief advantage is that it enables small samples to be distributed over a large surface area. This is particularly desirable in the present case because high rates of oxygen absorption are encountered. A uniform thickness of the aldehyde film was obtained by setting the vessel in a horizontal plane by a spirit level and inserting metal spacers between its lower surface and the bottom of the copper thermostat tank.

To assist dissolution of oxygen in the aldehyde the film was agitated by a glass-covered pin (length, 3 cm.) which was set in motion by a rotating magnetic field situated directly beneath the copper tank. This method of agitation was preferred to mechanical shaking because the latter would involve moving the reaction vessel to and fro in the light beam, thereby leading to periodic fluctuations in the intensity of the incident radiation.

FIG. 3.

Ultra-violet absorption spectrum of n-*decanal.*

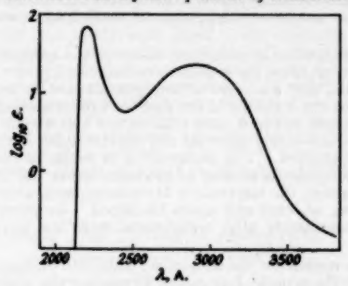


FIG. 4.

Transmission of Corning 597 R.P. Ultra glass filter.

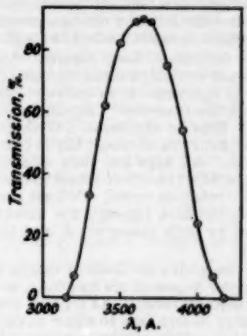
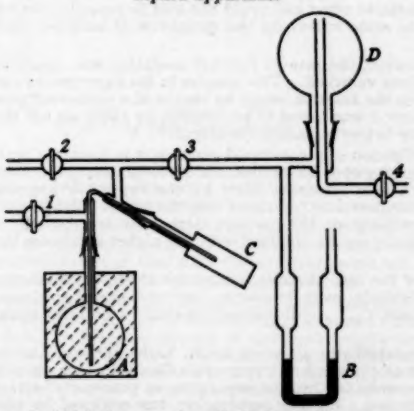


FIG. 5.

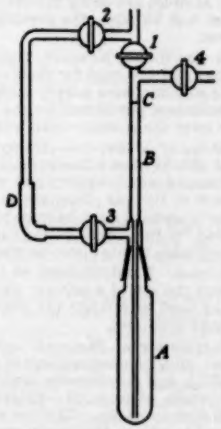
Siphon apparatus.



A, Aldehyde reservoir. *B, Safety valve.*
C, Reaction vessel. *D, Nitrogen reservoir.*

FIG. 6.

Constant-volume pipette.



Cleaning was normally carried out by repeated washing with absolute alcohol and pumping out under a high vacuum but, in the event of contamination with silicone tap grease, an alkali borate solution had to be used before the above treatment.

Optical Arrangement.—Absorption spectrum of n-*decanal.* There is no published information on the ultra-violet absorption of the longer-chain aliphatic aldehydes, so measurements were made on a Uvispec Spectrophotometer with solutions of *n*-decanal in *n*-decane. Beer's law was found to be obeyed and the calculated absorption curve for pure aldehyde is shown in Fig. 3.

Ultra-violet mercury lamp. The reaction vessel was illuminated from above, as shown in Fig. 1, the lamp used being of the G.E.C. "Osira" type stabilised by a constant-voltage transformer in

conjunction with the choke and condenser recommended by the makers. Another precaution taken to ensure constant intensity of illumination was to allow the lamp at least 45 minutes to come to equilibrium before readings were taken.

Light filter. From the extinction-coefficient measurements mentioned above, the degree of absorption at various wave-lengths which might be expected for the pure aldehyde under the experimental conditions may be calculated. Although the thickness of the liquid film never exceeded 1 mm., light of $\lambda < 3200$ A. is very strongly absorbed. To ensure that, as nearly as possible, the light absorption is even throughout the reacting system, a Corning 597 R.P. Ultra glass filter was interposed between the lamp and the reaction vessel. The transmission of this filter is given in Fig. 4.

Methods of Charging Reaction Vessel.—In view of the readiness with which aldehydes are oxidised in air, the liquid had to be introduced into the silica vessel without contact with the atmosphere. Direct vacuum-distillation was not practicable and alternative procedures adopted were as follows.

(a) *Siphon method.* The apparatus used is illustrated in Fig. 5. In order to charge the reaction vessel *C* with a sample of aldehyde, the weighed vessel *C*, already filled with nitrogen, is connected and a current of nitrogen is blown through it for a few minutes by opening taps 1, 3, and 4. These are then closed and, by cautiously opening tap 2, a quantity of aldehyde is drawn from *A* through the delivery tube into the reaction vessel *C*. Before the latter was removed for a second weighing, a stream of nitrogen is again passed through *D*, *C*, and *A*.

(b) *Constant-volume pipette.* Since (see below) the quantities of aldehyde taken in the samples are somewhat critical, another device (Fig. 6) was designed to measure out a definite volume of liquid. The mode of operation is as follows: Taps 1 and 3 are opened and a stream of nitrogen allowed to bubble through the reservoir. By closing of tap 1 and opening of tap 2 the air in the flexible rubber connection *D* may then be displaced. With *D* attached to the side-arm of tap 3, and with taps 3 and 4 open, the flow of nitrogen through tap 2 can be regulated so that the liquid rises up the pipette tube *B* to the mark *C*. All taps are then closed and tube *D* is disconnected. The reservoir *A* is replaced by the nitrogen-filled reaction vessel and when taps 1 and 3 are opened a stream of nitrogen forces the liquid into the reaction vessel. Whilst the flow of gas is maintained, the reservoir *A* is replaced, and, after the gas has bubbled through the aldehyde for a few minutes, all taps can again be closed. Stoppers are applied to both reservoir *A* and the reaction vessel immediately after withdrawal from the nitrogen stream.

In the above methods of taking aldehyde samples the reason for the somewhat elaborate precautions to prevent access of air has been, not so much to protect the sample, but rather to protect the reservoir of purified material. As regards the sample itself, exclusion of oxygen is not so important because it is necessary in any case to allow oxygen to come into contact with it for at least 5 minutes before readings of oxygen uptake can be commenced, in order that equilibrium conditions of temperature and dissolution of oxygen may be achieved. The relatively large rate of thermal oxidation at room temperature, however, does necessitate care in handling the reservoir of pure aldehyde. Successive exposures to air while samples are being taken would have a cumulative effect and could not lead to reproducible results for, as will be seen, the reaction rate depends to some extent on the quantities of oxidised material present.

It was found, however, that, in *n*-decane solution, the rate of thermal oxidation was considerably reduced and the need for these elaborate precautions vanished. The samples in the experiments carried out in solution were simply measured directly into the reaction vessel by means of a calibrated pipette, and sufficient protection for the liquid in the reservoir was found to be afforded by sweeping out the air space over the solution with nitrogen immediately before replacing the stopper.

Choice of Materials.—Aldehyde. In an investigation of a gas–liquid reaction it is desirable that the liquid should have a low vapour pressure. Pumping out of the system and introduction of the reactant gas become much easier, and complications such as a screening effect by the vapour or appreciable reaction in the gas phase are avoided. These considerations indicated that the higher members of the aliphatic series would be suitable materials. Furthermore, the reaction mechanism is not likely to be affected by the length of the carbon chain and hence results obtained with the higher aldehydes should be applicable to the lower members of the series.

Solvent. Establishment of the dependence of the rate of oxidation on the aldehyde concentration requires the use of a solvent which should be chemically inert, involatile, and transparent to the wave-lengths used to initiate the reaction. The aliphatic C_{10-15}-hydrocarbons seemed to be most suitable; *n*-decane was used.

Purification of Materials.—Aldehyde. *n*-Decanaldehyde, supplied by L. Light and Co. Ltd., was shaken, under an atmosphere of nitrogen, twice with 5% brine and twice with distilled water, then dried (Na_2SO_4), and fractionally distilled at reduced pressure in Quickfit apparatus, in presence of nitrogen, the fraction of b. p. 91—92°/10 mm. being collected. Further purification was achieved by further distillation *in vacuo*. The low vapour pressure at room temperature makes this extremely slow, but a reasonable rate of distillation was achieved by making use of tubing of 2-cm. diameter and keeping to a minimum the distance through which the vapour had to diffuse. Batches of approx. 20 c.c. were withdrawn from the reservoir of fractionated aldehyde by means of the siphoning device, and the dissolved gases removed by alternate freezing in liquid air and melting in a vacuum. Distillation *in vacuo* could then be carried from the temperature of the room to that of liquid air at a rate of about 20 c.c. in 24 hours. It was necessary to carry out 4—5 distillations before the aldehyde was pure enough to yield consistent rates of oxidation. Impure aldehyde left a white residue containing decanoic acid and probably some aldehyde polymer. During purification the liquid was shielded as much as possible from the light to minimise polymer formation, and all reservoirs were stored in the dark.

Solvent. *n*-Decane was shaken with concentrated sulphuric acid until the acid layer no longer darkened, and then with fuming sulphuric acid and fuming nitric acid, the same criterion of purity being

used. After treatment with 10% sodium hydroxide solution and distilled water (each 3 times) it was dried (Na_2SO_4) and fractionated under a reduced pressure of nitrogen. A few grams of sodium were added to the hydrocarbon before distillation to remove the last traces of water. At 15 mm., the *n*-decane boiled at 64·8—65·2°.

As a check the distillate was examined in a Grubb–Parsons Infra-red Spectrometer by Dr. G. M. Burnett: there was no trace of the absorption bands characteristic of unsaturated, carbonyl, or aromatic compounds. Some were detected, however, in the original material.

Results.

Preliminary Experiments.—Preliminary experiments carried out on aldehyde which had been fractionated but not distilled *in vacuo* showed that considerable thermal reaction took place at 25°. The rate of autoxidation was found to be sensitive to diffused daylight to a small extent and so the reaction system was enclosed in a light-proof cover. However, the thermal rate remained inconveniently large.

When dealing with a process of this kind, where both thermally and photochemically initiated reaction chains are propagating side by side, it is necessary to make certain assumptions regarding the relationship of the two in order to calculate what proportion of the overall rate measured under illumination is actually due to the light itself. For example, during his work on the photo-oxidation of aldehydes, Bäckström (*J. Amer. Chem. Soc.*, 1927, **49**, 1460) assumed that the photochemical and thermal rates were additive, but when the ratio of these quantities has a value as small as 1—2 large errors may be introduced by such an assumption. In order to reduce the proportion of the thermal reaction one can either reduce the working temperature or use an inert solvent. In the present instance, by working at high oxygen pressures (650 mm.) and low temperatures (5°), a value of 10 for the ratio of the photochemical to the thermal rate was obtained. However, further purification by repeated vacuum-distillation reduced this ratio to 5, owing to the greater sensitivity of the thermal process to impurity. Hence, thermal oxidation is still very prominent even at 5° and, since further reduction of

Fig. 7.

Dependence of the light rate on stirring speed.

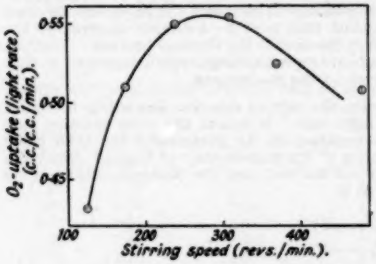
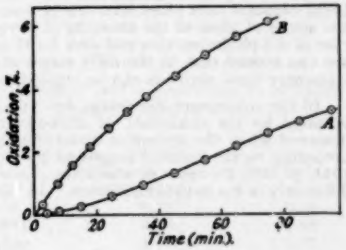


Fig. 8.

Course of thermal reaction at 5°.



the working temperature caused the reaction products to separate out of solution at inconveniently small extents of reaction, the ratio could not be increased in this way. A slight improvement could be effected by using an inert solvent.

Reproducibility to within $\pm 5\%$ was attained in the case of the photochemical and $\pm 10\%$ in the case of the thermal process. Further improvement was found to be impossible no matter how rigid the precautions taken, so that a number of experiments had to be carried out under identical conditions, and mean values of the rate measurements employed.

Rate of Dissolution of Oxygen.—Since the rates of oxygen uptake in this reaction are quite large it is important that the rate of dissolution of oxygen in the liquid should not be the rate-determining step. To ensure an adequate supply of dissolved oxygen an electromagnetic stirrer was employed and the sample size was kept to a minimum. Experiments were conducted to determine the effect of varying the stirring speed on the overall rate of oxygen uptake, and the results obtained are plotted in Fig. 7. It appears that, with stirring speeds above 350 revs./min., the uptake is lowered. The length of the stirring rod used was 2·5 cm. and its thickness 3 mm. so that the liquid surface was continuously being broken as the rods rotated. At the lower speeds, its action amounted to the transmission of waves across the aldehyde layer and so the whole sample was being subjected to disturbance. At the higher speeds, there was not sufficient time during a revolution for the aldehyde swept aside by the stirrer to be replaced and so the resultant effect was the formation of a circular hole in the film, the surrounding liquid being almost unaffected. As, therefore, the optimum rate of stirring appeared to be 300 revs./min., this value was selected as standard. Unfortunately, the onset of the phenomenon of hole-formation makes it impossible to tell whether, at this speed, the observed rates of oxidation are really independent of the rate of dissolution of oxygen. However, a consideration of the effect of sample size on the rate of reaction shows that this required condition is indeed satisfied.

It was found that, provided that the amount of aldehyde in the film did not exceed 2·5 c.c., the rate of oxygen uptake was independent of the quantity of material, other factors, *e.g.*, temperature, pressure, and stirring speed, being constant. Since the smallest amount of aldehyde that would maintain a

uniform film was 1·5 c.c., the experimental limits in this respect are somewhat narrow. Most of the work has been performed on 1·7-c.c. samples.

The General Course of the Reaction.—Some workers (*e.g.*, Raymond, *Compt. rend.*, 1922, **194**, 258) maintained that carefully purified aldehydes would not autoxidise at all or, at most, only after an induction period which could be shortened by irradiation with ultra-violet light. Hence, it was believed that heavy-metal catalysts or peroxides must be present before reaction would proceed. Further work has shown, however, that the methods of drying used in these experiments were likely to have introduced inhibitors into the system.

A general feature of autoxidation processes, namely, autocatalysis, is now well-established in the case of hydrocarbons, but with aldehydes at low temperatures this phenomenon does not seem to occur to any marked extent. Wieland and Richter (*Annalen*, 1931, **486**, 226) and Almquist and Branch (*J. Amer. Chem. Soc.*, 1932, **54**, 2293) report that, with benzaldehyde, a gradual decrease in the thermal rate at 25° takes place from the beginning of the reaction and, as far as the photo-process is concerned, Bäckström (*loc. cit.*) and Bowen and Tietz (*loc. cit.*) agree that a similar course is followed.

As regards the present work, we shall consider first the thermal reaction. Measurements of the oxygen uptake of incompletely purified samples indicated that, at low temperatures (5°), there was initially an induction period of a few minutes. This was followed by a gradual increase in rate to a maximum value; then it fell slowly until at 6% oxidation solid products of reaction began to separate from solution. Fig. 8, curve *A*, illustrates this behaviour, the % oxidation being calculated on the basis of one molecule of oxygen per molecule of aldehyde, as required for per-acid formation. Further purification of the aldehyde revealed that the apparent induction period must have been due to impurity for there was observed instead only a gradual decrease in reaction rate right from the initial stages (Fig. 8, Curve *B*).

For the photo-reaction at 5°, there was a similar gradual decay in the rate, the diminution not, however, taking place so rapidly. Once again, beyond 6% oxidation, separation of reaction products rendered stirring of the aldehyde film impossible and no reliance could be placed on rate measurements taken under these conditions.

Fortunately these changes in the reaction rates are not so rapid that the latter cannot be regarded as being constant over short intervals of time. It is therefore possible to calculate the rates directly from the slopes of plots of the amounts of oxygen absorbed against time over 3—4-minute intervals in the case of the photo-reaction and over 8—10-minute intervals in the case of the thermal process. Further, one can assume that, in the early stages of reaction, the radical concentrations remain constant, so that stationary-state methods can be applied to a kinetic analysis of the mechanism.

In the subsequent discussion, by "photo-rate" is meant the rate of reaction due solely to chains initiated by the absorption of ultra-violet light. By "light rate" is meant the total reaction rate observed when the system is under illumination. The calculation of the photo-rates has been made according to the method suggested by Noyes and Leighton ("Photochemistry of Gases," Reinhold, 1941, p. 198) for cases in which the chain mechanisms of the thermal and the photochemical process differ only in the mode of initiation. In these circumstances, if

$$\begin{aligned} \text{Thermal rate} &= R_T = \alpha T_i^n \\ \text{Photo-rate} &= R_P = \alpha I^n \\ \text{Light rate} &= R_L = \alpha(T_i + I)^n \end{aligned}$$

where T_i and I represent the rates of thermal and photochemical initiation, and α is a factor referring to the propagation and termination steps of the reaction, then it readily follows that:

$$(R_P)^{1/n} = (R_L)^{1/n} - (R_T)^{1/n}$$

The results of previous workers suggested that the value of n was $\frac{1}{2}$ and it will be seen that further justification of this value has been obtained.

Dependence of the Photo-rate on Light Intensity.—Variation of the light intensity was achieved by interposing perforated screens between the light source and the reaction vessel. Fine copper gauze, with its surface darkened by immersion in ammonium polysulphide to cut down reflection, was found to be suitable; its transmission was measured photoelectrically. To evaluate the intensity exponent, rates of oxygen uptake were measured over 3—4-minute periods (*a*) at full, (*b*) at reduced, and (*c*) at full intensity, the mean of (*a*) and (*c*) being taken as the full light rate. Determination of the thermal rate before and after illumination enabled also a mean value of this quantity to be obtained. Results showing that the photo-rate is dependent on the square-root of the absorbed light intensity are given in Table I.

Effect of Variation of the Oxygen Pressure.—(a) *Thermal reaction.* Owing to the great sensitivity of the thermal process to traces of impurity and the impossibility of obtaining better reproducibility than $\pm 10\%$, it is very difficult to establish the dependence of the reaction rate on oxygen pressures. The results shown in Table II indicate that the initial rate varies with the square-root of the oxygen pressure within the region investigated.

(b) *Photochemical reaction.* The effect on the photo-rate of altering the oxygen pressure is shown in Table III(*a*). Intensity-exponent measurements show by their tendency to fall below 0·5 that the values for the photo-rate at pressures lower than 600 mm. are not reliable and that under these conditions the rate of dissolution of oxygen is becoming the controlling factor. Hence, for pure *n*-decanal it is not possible to establish the dependence of the photo-rate on oxygen pressure.

TABLE I.

Dependence of the photo-rate on light intensity.

(Rates expressed in mol./l.sec., × 10^4.)

Mean full photo-rate.	Reduced photo-rate.	Transmission of screen (%).	Intensity exponent.
3·92	2·06	30·6	0·54
4·23	2·39	30·6	0·48
4·06	2·35	30·6	0·46
4·14	2·70	41·6	0·49
4·18	2·77	41·6	0·47
4·19	2·71	41·6	0·52
		Mean	0·49

TABLE II.

Dependence of initial thermal rate on oxygen pressure. Temp., 5°.

Pressure (p) (mm.).	$p^{\frac{1}{2}}$.	Rate (mol./l.sec., × 10^6).	$p^{\frac{1}{2}}$/Rate.
700	26·4	10·4	2·54
650	25·5	9·95	2·56
600	24·5	9·1	2·69
550	23·4	8·5	2·76
500	22·4	8·2	2·73
450	21·2	7·6	2·79
350	18·7	7·0	2·67

TABLE III.

Dependence of initial photo-rate on oxygen pressure.

Pressure (mm.).	Rate (mol./l.sec., × 10^4).	Intensity exponent.	Pressure (mm.).	Rate (mol./l.sec., × 10^4).	Intensity exponent.
(*a*) *Pure aldehyde. Temp.*, 5°.			(*b*) 30% *Solution of aldehyde in decane. Temp.*, 10°.		
700	4·44	0·51	700	2·11	0·55
650	4·32	0·49	650	2·14	0·51
600	4·35	0·48	550	2·07	0·54
550	4·01	0·46	450	1·92	0·52
450	3·66	0·42	350	1·77	0·45
350	3·32	0·40			

TABLE IV.

Dependence of initial thermal rate on aldehyde concn. Temp., 10°.

Aldehyde concn. (c) (mol./l.).	$c^{3/2}$.	Rate (mol./l.sec., × 10^5).	$c^{3/2}$/Rate.
0·53	0·38	0·45	0·8
1·58	2·00	1·34	1·5
2·63	4·27	2·68	1·6
3·67	7·08	6·42	1·1
5·25	12·30	11·4	1·1

TABLE V.

Dependence of initial photo-rate on aldehyde concn. Temp., 10°.

Aldehyde concn. (c) (mol./l.).	Rate (mol./l.sec., × 10^4).	c/Rate.
0·53	0·61	0·87
1·58	2·28	0·69
2·63	3·86	0·68
3·67	4·64	0·79

However, some experiments carried out with 30% solutions of the aldehyde in *n*-decane show that over the range 400—700 mm. variation of the oxygen pressure does not affect the photo-rate [Table III(*b*)].

Effect of Variation of the Aldehyde Concentration.—Experiments with *n*-decane solutions to determine the dependence of the thermal reaction rate on aldehyde concentration also showed rather poor reproducibility, and mean values had again to be taken from a number of determinations under identical conditions. As can be seen from Table IV the reaction rate appears to be proportional to (aldehyde concentration)$^{3/2}$. The corresponding data for the photo-process (Table V) show that the photo-rate depends on the first power of the aldehyde concentration. The results of these experiments in solution provide no evidence that *n*-decane interferes in any way with the propagation of the autoxidation chains, *e.g.*, as shown in Table III the intensity exponent still has a value of 0·5.

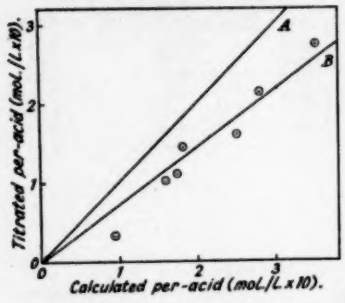
Estimation of Per-acid.—During his work on benzaldehyde autoxidation, Bäckström (*Medd. K. Vet. Nobelinst.*, 1927, **6**, 15, 16) determined the concentration of perbenzoic acid in the reaction mixture by the iodine–thiosulphate method. Although the observed amounts of per-acid always fell below the value expected on the basis of the oxygen absorbed, yet the deficiency could be explained quantitatively as being caused by formation of benzoic acid by the reaction of some of the per-acid with further aldehyde.

To ensure that a similar situation exists in the present instance, the amount of perdecanoic acid present at various extents of oxidation was determined. The method adopted has been developed from those of Bäckström (*loc. cit.*) and Kolthoff (*J. Polymer Sci.*, 1947, **2**, 199). Measurements of the oxygen uptake were made on the manostat in the usual manner. The reaction was stopped at different percentages of oxidation and a mixture of 10% aqueous potassium iodide (10 c.c.) and 0·4N-acetic acid (5 c.c.) introduced immediately. Sufficient alcohol was added to give a homogeneous solution which was transferred quantitatively (by several washings with alcohol) to a flask through which a steady stream of nitrogen was flowing. The free iodine was then determined with 0·02N-sodium thiosulphate. Further addition of alcohol to maintain homogeneity was made whenever necessary. The presence of

alcohol makes it impossible to use starch solution, but the disappearance of the colour of the iodine itself was sharp enough to give satisfactory results (±0·05 c.c.). All solutions and solvents used in this determination were stored under nitrogen and a stream of the gas was passed through them before they came into contact with the autoxidised sample.

FIG. 9.

Per-acid concentration at 5°.



Per-acid concentrations determined for several samples are shown in Fig. 9, curve *B*, plotted against the concentration expected from the amounts of oxygen absorbed. If the per-acid did not react further with the aldehyde line *A* would be obtained, but a comparison of the two slopes indicates that over the region examined 72% of the per-acid formed remains as such in the reaction mixture. Exact estimates of the total oxygen uptake are not easy to obtain because of the necessary time-lag which must be allowed for temperature equilibrium to be reached before taking readings on the monostat.

The reaction between per-acid and iodide may be represented by $R{\cdot}CO{\cdot}OOH + 2I^- + H^+ \longrightarrow R{\cdot}COO^- + I_2 + H_2O$, so one equivalent of per-acid corresponds to 2 equivs. of thiosulphate. The per-acid content has been calculated by use of this relationship.

It is not possible to calculate from the above results an exact value of the velocity constant for the pseudo-unimolecular secondary reaction of per-acid with aldehyde, owing to the limited region over which the measurements have been made. However, this may be estimated to be of the order 10^{-6}, which agrees with the 10—30-minute half-periods found for the corresponding reaction with benzaldehyde and acetaldehyde by Bäckström (*loc. cit.*) and Kagan and Lubarsky (*J. Phys. Chem.*, 1935, **39**, 847).

DISCUSSION.

That the autoxidation of aldehydes proceeds by a radical chain mechanism was clearly indicated by Bäckström (*Z. physikal. Chem.*, 1934, **25**, *B*, 99). The results presented above show that, under the somewhat limited conditions in which experiment is possible, the following empirical equations may be written for the initial thermal and photo-rates of autoxidation:

$$R_T = k'[R{\cdot}CHO]^{3/2} \cdot [O_2]^{\frac{1}{2}} \quad \ldots\ldots\ldots (1)$$

$$R_P = k''[R{\cdot}CHO] \cdot [O_2]^0 \cdot I^{\frac{1}{2}} \quad \ldots\ldots\ldots (2)$$

where I is the effective light intensity. The kinetic evidence is more reliable in the case of the photo-process because of the greater accuracy which could be achieved in the rate measurements.

It has been assumed, in calculating the photo-rates, that the mechanisms of both the thermal and the photochemical process are identical except for the initiation step. If the assumption had been made that the mechanism of the thermal and photo-processes were different, then direct subtraction of the thermal from the light rate would give the corresponding photo-rate, *i.e.*, $R_P = R_L - R_T$. If calculations of the intensity exponent are made from photo-rates derived in this way, then values consistently higher than 0·5 are obtained no matter how pure the aldehyde samples may be. For example, by this method the last result in Table I gives an intensity exponent of 0·69. Since the aldehyde used had been carefully purified, this value cannot be explained as being due to the presence of chain-breaking impurities, and so it seems that the assumptions made about the relative mechanisms of the two reactions are correct.

It is clear from the square-root dependence on the light intensity that the reaction chains are being terminated by the mutual destruction of two radical chain carriers. If this is also the case in the thermal process, then R_T must depend on $T_i^{\frac{1}{2}}$ where T_i is the rate of thermal initiation. Hence, if the reaction chains started thermally commence by some type of interaction of the aldehyde with oxygen, this process may be represented as

$$R{\cdot}CHO + O_2 \longrightarrow \text{chain carriers}$$

and a term $[R{\cdot}CHO]^{\frac{1}{2}}[O_2]^{-\frac{1}{2}}$ would be included in the overall thermal rate expression. If (1) is rewritten as:

$$R_T = k'[R{\cdot}CHO][O_2]^0[R{\cdot}CHO]^{\frac{1}{2}}[O_2]^{\frac{1}{2}} \quad \ldots\ldots\ldots (3)$$

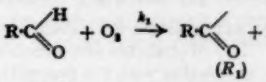
it can be seen that, apart from the contribution of the initiation process, the expressions for the thermal and photo-rates become identical. Thus there is a strong likelihood that the subsequent steps are the same in the two cases.

From the general nature of the course of reaction, which shows no sign of autocatalysis in either the thermal or the photo-chemical process at low temperature provided that pure materials are used, it would seem that the products do not participate in the initiation of reaction chains in contrast to olefinic and hydroaromatic autoxidation products. Thus, initiation

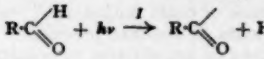
reactions must be postulated which do not involve the per-acid. The kinetic evidence points to a process involving the direct interaction of the aldehyde and oxygen although the exact nature of such a step must necessarily remain somewhat speculative at the moment.

The mechanism suggested to account for the above observations is :

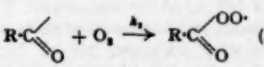
Initiation :

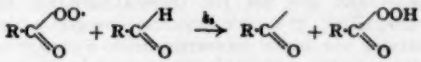
Thermal :  (*a*)

(R_1)

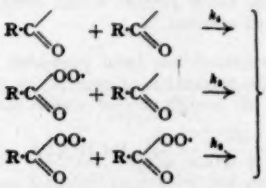
Photochemical :  (*b*)

Propagation :

 (R_2) (*c*)

 (*d*)

Termination :

 Inert products (*e*), (*f*), (*g*)

If it is assumed that (*a*) the concentrations of the chain carriers reach stationary values, (*b*) the reaction chains are long so that the rates of the initiation and termination steps become negligible in comparison with those of propagation, and (*c*) at the relatively high oxygen pressures used the addition of oxygen to aldehyde radicals takes place much more rapidly than the abstraction of hydrogen by the peroxide radicals, and, consequently, that processes (*e*) and (*f*) may be neglected, then the above scheme gives for the overall reaction rate :

$$-\frac{d[O_2]}{dt} = \frac{k_2[R\cdot CHO]}{\sqrt{k_6}}(I + k_1[R\cdot CHO][O_2])^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad (4)$$

which gives :

$$R_T = \sqrt{k_1}\frac{k_2}{\sqrt{k_6}}[R\cdot CHO]^{3/2}[O_2]^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

$$R_T = \frac{k_2}{\sqrt{k_6}}[R\cdot CHO]I^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

Expressions (5) and (6) are seen to agree with the empirical equations (1) and (2).

It makes no difference to the final result in the above scheme whether R_1 or R_2 is produced by the thermal initiation process, but R_1 would be the more likely. The exact mechanism of the photo-initiation step is not known, but evidence from studies of the photo-decomposition of aldehydes indicates that absorption of near ultra-violet radiation can bring about formation of R_1 radicals (Noyes and Leighton, *op. cit.*, p. 238).

From the great length of the reaction chains encountered here, it follows that the proportion of the products of the termination step in the resulting mixture will be very small. No attempt has been made to identify these materials.

Since the autoxidation of *n*-decanal, whether thermal or photochemical, proceeds by a chain mechanism involving termination by the mutual removal of the chain carriers, the reaction satisfies the conditions which must be fulfilled before methods similar to those of Burnett and Melville (*Proc. Roy. Soc.*, **1947**, *A*, **189**, 456) can be applied in order to obtain absolute values of the velocity coefficients for the propagation and termination steps. The results of such measurements are given in the following paper.

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM, 15.

[*Received, January 10th*, 1951.]

445. *The Kinetics of the Autoxidation of* n-*Decanal. Part II.* The Velocity Constants.*

By H. R. Cooper and H. W. Melville.

The retardation of the autoxidation of *n*-decanal by small amounts of quinol has been studied. The overall-reaction kinetics of the system show that the retarder operates by reacting with the peroxidic radicals. A method is described whereby the rate of chain initiation, R_i, can be calculated from the rates of oxygen absorption at constant pressure.

Application of the method of intermittent illumination to the unretarded reaction enables the chain life, τ, to be measured. From R_i and τ, along with the thermal-, photo-, and retarded-reaction rates, it is possible to obtain absolute values of the velocity constants for all the processes involving peroxidic radicals and also for the thermal-initiation step. Owing to experimental difficulties, the corresponding energies of activation were obtained by carrying out similar measurements in *n*-decane solution. When coupled with the velocity coefficients determined in the pure liquid, these give rise to frequency and steric factors which compare favourably with published values for related systems.

In the preceding paper, kinetic evidence has been presented which enabled a free-radical mechanism to be established for the formation of peracid by the autoxidation of *n*-decanal. The equation deduced to represent the overall rate of oxygen absorption was of the form:

$$-\frac{d[O_2]}{dt} = \frac{k_3}{\sqrt{k_6}}[R{\cdot}CHO]R_i^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

and it can be seen that, if some method of determining the rate of initiation, R_i, is available then the ratio of the velocity constants for propagation and termination, $k_3/k_6^{\frac{1}{2}}$, can be found.

Under the experimental conditions for which equation (1) holds, *i.e.*, at high oxygen pressures, the addition of oxygen to the aldehydic radicals is considered to occur so much more rapidly than the abstraction of hydrogen atoms by the peroxidic radicals that it takes up a negligible part of the time of one chain cycle. The lifetime of the kinetic chain may therefore be represented by $\tau = \nu\bar{\tau}$, where ν is the chain length and $\bar{\tau}$ is the mean time required for a peroxidic radical to dehydrogenate an aldehyde molecule. The fate of the peroxidic radicals is the sole factor determining the chain lifetime which can be expressed in the form:

$$\tau = \frac{\text{Concentration of peroxidic radicals}}{\text{Rate of removal of peroxidic radicals}} = \frac{1}{k_6[R_2]} \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $[R_2]$ represents the concentration of the peroxidic radicals. From the reaction mechanism quoted in the preceding paper it follows that, under stationary-state conditions, $R_i - k_6[R_2]^2 = 0$. Substituting for $[R_2]$ in (2), we have

$$\tau = 1/\sqrt{k_6 R_i} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

It follows from (1) and (3) that:

$$k_3 = R_L/(\tau[R{\cdot}CHO]R_i) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

$$k_6 = 1/\tau^2 R_i \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

and hence, if R_i and τ are known, then absolute values of k_3 and k_6 can be found.

The Rate of Initiation.—It has been shown by Burnett and Melville (*Proc. Roy. Soc.*, 1947, *A*, **189**, 456) that the rate of initiation in the photopolymerisation of vinyl acetate may be measured by following the course of the reaction inhibited by benzoquinone. In this case, polymerisation was stopped completely by the inhibitor for lengths of time which were dependent on the inhibitor concentration, and so, by measuring these induction periods it was possible to estimate the rate of removal of benzoquinone and hence to obtain the rate of chain initiation.

With autoxidising systems, however, only high inhibitor concentrations will stop the reaction completely. Furthermore, the length of the induction period is not easy to assess,

* Part I, preceding paper.

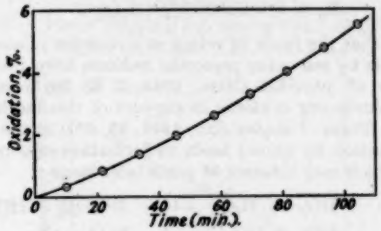
because there is no sudden onset of reaction; instead, a gradual increase in the rate of oxygen absorption occurs as the concentration of antioxidant diminishes.

Fortunately, it has proved possible to find the rate of initiation by following the course of autoxidation in the presence of low concentrations of a retarder. The material used was quinol, recrystallised three times from water under an atmosphere of nitrogen. Complications caused by internal filter effects cannot occur with this substance for, as shown by Klingstedt (*Compt. rend.*, 1922, **175**, 366), the molecular extinction coefficient of quinol falls to zero at 3180 A. and remains at this value over the whole region transmitted by the Corning 597 R.P. Ultra glass filter.

The Course of the Retarded Reaction.—By using quinol concentrations of the order of 10^{-4} mole per litre, oxygen absorption was found to follow the course shown in Fig. 1, a gradual

FIG. 1.

The course of photo-oxidation retarded by quinol at 5°.



increase in reaction rate being observed. As in other experiments (preceding paper), the separation of the products from solution prevented the process from being followed beyond 6% oxidation at 5°.

Dependence of the Rate on Quinol Concentration.—In order to establish the dependence of the reaction rate on quinol concentration it is necessary to have some means of extrapolating back to the time when measurements of the oxygen absorption were commenced. The method of extrapolation employed has been to plot the reciprocal of the rate against time and to find the intercept at zero time.

TABLE I.

Dependence of the retarded rate on quinol concentration.

Temp., 5°. Oxygen pressure, 650 mm.

Initial quinol concn., $[H_2Q]_0$ (mol./l. × 10^5).	$\frac{1}{10^4[H_2Q]_0}$.	Initial retarded rate, R_{R_0} (mol./l.sec., × 10^6).	$R_{R_0} \times [H_2Q]_0 \times 10^9$.
3·16	3·17	7·40	2·34
5·43	1·84	4·95	2·69
6·10	1·64	3·95	2·41
7·40	1·35	3·50	2·59
42·80	0·23	0·82	3·51

The corresponding uninhibited rate was $4{\cdot}40 \times 10^{-4}$ mol./l./sec.

TABLE II.

Dependence of retarded rate on the light intensity.

Temp., 5°. Oxygen pressure, 650 mm.

$[H_2Q]_0$ (mol./l. × 10^5).	Mean rate at full intensity (mol./l.sec., × 10^6).	Rate at reduced intensity (mol./l.sec., × 10^6).	Transmission of screen (%).	Intensity exponent.
3·16	9·56	4·26	41·6	0·93
6·10	6·25	2·73	41·6	1·02
7·40	4·05	1·62	41·6	1·05
42·80	1·34	0·55	41·6	0·95
				Mean 0·99

Estimates of the initial rates of oxygen absorption obtained in this way are shown in Table I and the results indicate that the retarded rate is inversely proportional to the retarder concentration.

Dependence of the Rate on Light Intensity.—The method used was identical with that employed to establish the dependence of the uninhibited process on the light intensity. The results quoted in Table II indicate that a first-power relationship holds in this case.

Dependence of Rate on Aldehyde Concentration and Oxygen Pressure.—No experiments were carried out in the present instance to establish the relationship between the rate of the retarded reaction and the aldehyde concentration or oxygen pressure, but Bowen and Tietz (*J.*, 1930, 234) showed that for acetaldehyde oxidation retarded by alcohol:

$$\text{Retarded rate} \propto [\text{R·CHO}]^1[\text{O}_2]^0$$

Mechanism of the Retarded Reaction.—The above results lead to an empirical expression for the retarded reaction rate of the form:

$$R_2 = k[\text{R·CHO}]^1[\text{O}_2]^0[\text{H}_2\text{Q}]^{-1}I \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

It is now well established that the mode of action of a retarder in stopping autoxidation chains at high oxygen pressures is by removing peroxidic radicals from the system. This conclusion was reached by Bäckström (*Z. physikal. Chem.*, 1934, *B*, **25**, 99) from his work with aldehydes, and recently even more convincing evidence in support of this mechanism has been presented by Bolland and ten Have (*Trans. Faraday Soc.*, 1947, **43**, 201) in the case of the olefins. They suggest that chain termination by quinol leads to formation of a comparatively stable semiquinone radical, two of which may interact at some later stage:

$$\text{RO}_2\text{–} + \text{H}_2\text{Q} \longrightarrow \text{RO·OH} + \text{HQ–}$$
$$\text{HQ–} + \text{HQ–} \longrightarrow \text{H}_2\text{Q} + \text{Q}$$

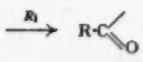
On this basis, each quinol molecule can terminate two reaction chains. That a similar state of affairs holds true in the autoxidation of *n*-decanal is supported by the appearance of a slight yellow colour in the reaction mixture after a sample containing quinol has been exposed to oxygen under ultra-violet radiation.

It was observed that, even with such low quinol concentrations, thermal autoxidation was reduced to such small proportions as not to be measurable under the experimental conditions. A given amount of retarder would be expected to have more effect on the thermal than on the photochemical process because the chain length is much longer in the former case. Hence, the thermal reaction can be neglected in calculations concerning the retarded rates of oxidation. Moreover, it is the total rate of initiation under illumination that these experiments are designed to measure.

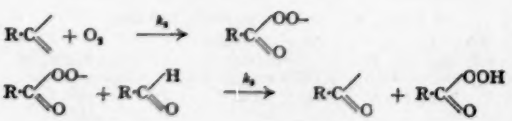
The gradual increase in reaction rate in presence of quinol cannot be attributed to the action of autoxidation products derived from the aldehyde, for autocatalysis is not encountered with the uninhibited material. The products derived from the retarder, quinonoid in type, would not be expected to catalyse the process and, in fact, have been shown (Bolland and ten Have, *loc. cit.*) to be very weak retarders themselves. Hence the acceleration of the oxygen absorption may be attributed solely to the consumption of quinol in stopping chains. The non-interference of the products has been assumed in the evaluation of the rate of initiation.

The mechanism of the retarded oxidation would therefore be simply:

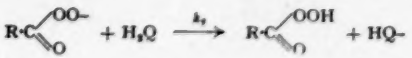
Initiation:



Propagation:



Termination:



Assuming that, over short intervals, the concentration of the radicals remains sensibly constant, we have from this scheme:

$$-\frac{d[O_2]}{dt} = R_i\left(1 + \frac{k_3[R\cdot CHO]}{k_7[H_2Q]}\right)$$

Now, at low inhibitor concentrations the chain length is still quite large and so the rate of initiation will be small in comparison with the overall rate of oxygen absorption. Taking into account the relative magnitudes of R_i and $-d[O_2]/dt$, we may write for the retarded rate:

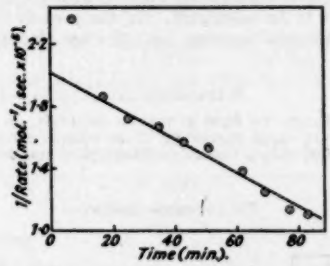
$$R_R = R_i k_3[R\cdot CHO]/k_7[H_2Q] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

which obviously has the same form as the empirical equation (6).

Determination of the Rate of Initiation.—If we still assume that the radical concentration remains sensibly constant and that one quinol molecule can stop two reaction chains, it follows

FIG. 2.

The retarded reaction at 5°. Plot of reciprocal rate against time: $[H_2Q]_0 = 5{\cdot}43 \times 10^{-4}$ *mol./l.*



that the rate of removal of quinol is given by $-d[H_2Q]/dt = R_i/2$. On integration, with the limiting condition that at $t = 0$, $[H_2Q] = [H_2Q]_0$, this gives $[H_2Q] = [H_2Q]_0 - \frac{1}{2}R_i t$. On substitution in (7) for $[H_2Q]$, we have,

$$R_R = \frac{k_3[R\cdot CHO]R_i}{k_7([H_2Q]_0 - \frac{1}{2}R_i t)}$$

hence

$$\frac{1}{R_R} = \frac{k_7[H_2Q]_0}{k_3[R\cdot CHO]R_i} - \frac{k_7 t}{2k_3[R\cdot CHO]}$$

Therefore it would be expected that a plot of $1/R_R$ against t would be a straight line. Further, we have

$$\frac{\text{Slope}}{\text{Intercept}} = \frac{R_i}{2[H_2Q]_0}$$

and since $[H_2Q]_0$ is known, R_i, the rate of initiation, may be calculated.

Fig. 2 illustrates an example of the type of $1/R_R$–t plot obtained. It was always observed that in the very early stages of reaction the value of $1/R_R$ was too large. The experimental difficulties in accurately measuring rates of oxygen absorption are very great, but the displacement is too large to be accounted for by experimental error. This discrepancy has been neglected in extrapolating back to zero time.

Table III shows the results of determinations of the rate of initiation which have been made in this way for a number of different initial quinol concentrations. The mean value of $1{\cdot}1 \times 10^{-7}$ mol./l.sec. is a weighted mean based on the number of determinations made at each concentration of quinol. To show that the reaction chains are still quite long under the experimental conditions, values of the initial chain lengths are also included, calculated from $\nu_0 = R_{R_0}/R_i$. $R_i = 1{\cdot}1 \times 10^{-7}$ mol./l.sec. will be a mean value for the thermally and photochemically initiated processes since the rate of initiation determined is a composite one: $R_i = k_1[R\cdot CHO][O_2] + I$.

The Chain Lifetime.—A method of determining this quantity by irradiating the system with an intermittent illumination is mentioned by Noyes and Leighton (" Photochemistry of

TABLE III.

The rate of initiation.

Temp., 5°. Oxygen pressure, 650 mm.

$[H_2O]_0$ (mol./l. × 10^5).	Initial rate, R_{i_0} (mol./l.sec., × 10^5).	$\frac{\text{Slope}}{\text{Intercept}} = \frac{R_i}{2[H_2O]_0}$.	R_i (mol./l.sec., × 10^5).	ν_0.
3·16	7·40	14·80	9·4	675
5·43	4·95	9·74	10·6	450
7·40	3·50	7·86	11·6	360
42·80	0·82	1·71	14·6	75
			Mean 11·0	

Gases," p. 202, Reinhold, 1941) and has been successfully applied to the polymerisation of vinyl compounds by Burnett and Melville (*loc. cit.*) and others and more recently to the autoxidation of olefins by Bateman and Gee (*Proc. Roy. Soc.*, 1948, *A*, **195**, 376). Measurements of reaction rates at a number of different flashing speeds, with the application of an appropriate theoretical treatment, enable τ to be calculated. In the present instance, due allowance must be made for the background thermal reaction, and this has already been shown to be possible by Bateman and Gee.

EXPERIMENTAL.

Apparatus.—In order to interrupt the light at regular intervals, an automatic shutter mechanism was constructed which gave a very rapid movement of an opaque screen across the light beam. By using a Megatron photocell coupled with a Cossor Oscillograph it was found that the time required for

FIG. 3.

The automatic shutter.

the movement of the arm was less than 20 millisecs. The method of operation of this shutter is illustrated in Fig. 3, where it can be seen that, by energising coil *A* all the time and the larger coil *B* intermittently, the light metal plates *D* are attracted in turn and the duralumin shutter arm *S* oscillates pivoting on shaft *C*. Regularity of the movement was achieved by passing the current to coil *B* through commutators rotated at a constant speed by a gramophone motor. The range of the instrument (flash times of 0·25—25 secs.) was increased by variation of the number of segments on the commutators and also by suitable reduction gearing.

Determination of the Lifetime.—The theory of intermittent illumination requires that the reaction system should satisfy certain conditions: (*a*) The reaction must be a chain process, capable of being initiated photochemically. (*b*) The mechanism of the thermal and photo-reactions must be the same apart from the initiation step. (*c*) The photo-rate must not be dependent on the first power of the light intensity. (*d*) The absorption of the light must take place uniformly throughout the reaction medium. (*e*) The interruption of the light beam must be instantaneous so that scanning of the reaction vessel does not occur.

Conditions (*a*), (*b*), and (*c*) have been shown to be satisfied in the autoxidation of *n*-decanal. The glass filter ensured that the wave-lengths initiating the photo-reaction were only weakly absorbed, and the shutter device was designed to move quickly enough to satisfy condition (*e*) over the range of flash times investigated.

Mathematical treatment of the system along the lines suggested by Bateman and Gee (*loc. cit.*) and Matheson (*J. Amer. Chem. Soc.*, 1949, **71**, 497 gives:

$$\gamma = \frac{1+\omega}{2} + \frac{1}{2K} \ln \frac{(1+x)(1+y/\omega)}{(1+y)(1+x/\omega)} \quad \ldots\ldots\ldots\ldots (8)$$

where

$$\gamma = \frac{\text{light rate under intermittent illumination}}{\text{light rate at full intensity}}$$

$$\omega = \frac{\text{thermal reaction rate}}{\text{light rate at full intensity}}$$

$K = k_5[R_2]\,\theta$, $x = [R_2]_1/[R_2]_s$, $y = [R_2]_2/[R_2]_s$, θ = flash time (in sec.)

$[R_2]_0$, $[R_2]_1$, and $[R_2]_2$ are the concentrations of peroxidic radicals in the system respectively under steady illumination, at the beginning of the light period, and at the end of the light period; x and y in the above equation can be expressed in terms of K by the solution of :

$$ay^2 + by - c = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

$$ax^2 - bx - c = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

where

$$a = \tanh \omega K + \omega \tanh K$$

$$b = (\omega^2 - 1)\tanh K \tanh \omega K$$

$$c = \omega (\tanh K + \omega \tanh \omega K)$$

Substitution of the expressions obtained for x and y from (9) and (10) in (8) enables γ to be written in terms of a single variable quantity, K, but it is not possible to rearrange the resulting equation so that K can be calculated from the readily measured ratios γ and ω. However, if a series of values are given to K, then the corresponding values of γ can be calculated. The limiting values can be obtained from :

$$\gamma_{\theta \to \infty} = \frac{1 + \omega}{2} \quad \gamma_{\theta \to 0} = \left\{\frac{1 + \omega^2}{2}\right\}^{\frac{1}{2}}$$

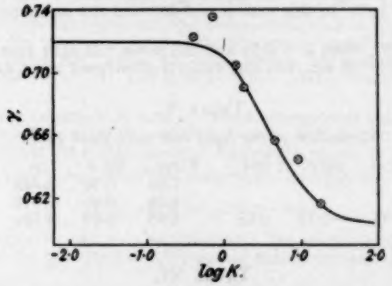
A curve relating γ and log K may then be plotted, the general form of which is shown in Fig. 4. If the experimental values of γ obtained at different flash times are plotted on the same scale, then since

$$\log \theta - \log K = \log \frac{1}{k_4[R_2]_0} = \log \frac{1}{\sqrt{k_4 R_i}} = \log \tau$$

the lifetime, τ, may be calculated by measuring the distances of the experimental points from the theoretical curve along lines of constant γ.

FIG. 4.

Determination of chain lifetime at 5° : $\omega = 0{\cdot}20$.



Results.—The procedure adopted in measuring γ was to compare the light rate under intermittent illumination with the mean value of the full light rates determined immediately before and after the latter. For pure n-decanal at 5° the value of ω is 0·2, based on the mean value of the thermal rates before and after the light rate measurements. The theoretical curve for $\omega = 0{\cdot}2$ and the experimental points from Table IV are both plotted in Fig. 4.

TABLE IV.

Variation of light rate with flash time.

θ (sec.).	log θ.	γ.	log K.	log θ − log K = log τ.	τ (sec.).
0·42	−0·38	0·723	—	—	—
0·74	−0·13	0·736	—	—	—
1·45	0·16	0·705	0·100	0·06	1·15
1·84	0·265	0·691	0·280	−0·015	0·97
4·58	0·66	0·657	0·652	0·008	1·02
9·10	0·96	0·645	0·790	0·17	1·48
17·60	1·25	0·617	1·250	0·00	1·00
					Mean 1·10

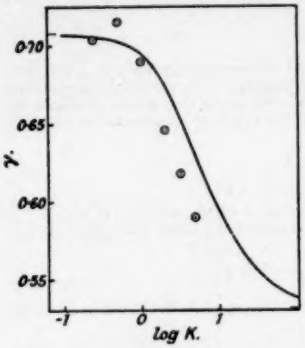
The points in Fig. 4 from which the lifetime of 1·1 sec. has been determined are, as usual, mean values of several observations at each flashing speed; log K was read off the theoretical curve corresponding to the measured values of γ. The mean value of the light rate was $4{\cdot}40 \times 10^{-4}$ mol./l./sec.

The Reaction in Solution.—In order to obtain the energies of activation of the individual radical processes it is necessary to measure reaction rates, lifetimes, etc., at a minimum of two different temperatures. Unfortunately, in the present case, a temperature increase of more than 5° led to rates of

oxygen absorption which were dependent on rates of solution in the aldehyde, and a temperature decrease of more than 5° led to similar difficulties owing to the rapid separation of reaction products. Variation of the temperature within the experimental limitations encountered in the autoxidation of pure *n*-decanal, therefore, cannot lead to values of the activation energies which are sufficiently reliable to have any significance.

FIG. 5.

Determination of chain lifetime at 10° in 30% n-decane solution: $\omega = 0{\cdot}062$.



In Part I (preceding paper), the results of some experiments in *n*-decane solution were presented in connection with the dependence of the reaction rate on the aldehyde concentration and the oxygen pressure. These experiments indicated that the solvent did not seriously interfere with the propagation of the reaction chains, and, since reliable rates of oxygen uptake could be obtained over a much wider temperature range in solution, measurements of rates of initiation and chain lifetimes were carried out at 10° and 26° with 30% solutions of *n*-decanal in *n*-decane. At both temperatures, the intensity exponent remained at 0·5 for the unretarded reaction, showing that the observed rates were independent of the rate of solution of oxygen throughout.

Rates of Initiation.—In the presence of quinol the oxygen absorption of 30% solutions in decane showed similar behaviour to that observed with pure aldehyde, the reaction rate steadily increasing as the retarder was consumed. Calculation of the rates of initiation, therefore, could again be made by the method already described. The initial quinol concentration was $3{\cdot}18 \times 10^{-4}$ mol./l. Extrapolation of the linear plots of reciprocal rate against time gave, for Slope/Intercept $= R_i/2[H_2Q]_0$: at 10° $1{\cdot}3 \times 10^{-4}$ sec.$^{-1}$; at 26°, $1{\cdot}4 \times 10^{-4}$ sec.$^{-1}$. Hence $R_i = 8{\cdot}3 \times 10^{-8}$ and $9{\cdot}1 \times 10^{-8}$ mol./l.sec. at 10° and 26°, respectively.

Chain Lifetimes.—The procedure adopted in determining the chain lifetimes was identical with that in the case of the pure aldehyde. The results given in Table V and plotted in Fig. 5 show that τ has a value of 0·6 sec. at 10°. In this case $\omega = 0{\cdot}062$ and the mean full light rate was $2{\cdot}3 \times 10^{-4}$ mol./l.sec.

Similar experiments at 26°, when $\omega = 0{\cdot}14$ and the mean full light rate was $3{\cdot}4 \times 10^{-4}$ mol./l.sec., gave a mean chain lifetime of 0·66 sec., but this value is considered to be within experimental error the same as that at 10°.

TABLE V.

Variation of the light rate with flash time.

θ (sec.).	log θ.	γ.	log K.	log τ.	τ (sec.).	θ (sec.).	log θ.	γ.	log K.	log τ.	τ (sec.).
0·244	−0·61	0·704				1·96	0·30	0·646	0·54	−0·24	0·58
0·485	−0·31	0·715				3·26	0·50	0·618	0·78	−0·28	0·52
1·000	0	0·690	0·11	−0·11	0·78	4·63	0·69	0·590	1·04	−0·35	0·45
											Mean 0·6

TABLE VI.

Energies of activation.

Process.	Rates of oxidation (mol./l.sec., × 10^8): at 10°.	at 26°.	Energy of activation (kcals.).
Thermal.			
Pure aldehyde	11·7	39·1	$E_T = 12{\cdot}8$ } Mean
In solution	1·37	3·59	$E_T = 10{\cdot}2$ } 11·5
Photochemical.			
In solution	22·8	33·7	$E_P = 3{\cdot}7$
Inhibited.			
In solution	0·91	1·41	$E_R = 4{\cdot}8$
Initiation.			
In solution	0·0083	0·0091	$E_i = 1{\cdot}0$

Energies of Activation.—In Table VI are presented the results of measurements of the various autoxidation rates at corresponding extents of reaction in solution at 10° and 26°. The energies of activation are calculated on the assumption that the Arrhenius law is obeyed.

From the appropriate rate expressions:

$$E_T = \tfrac{1}{2}E_1 + E_2 - \tfrac{1}{2}E_6$$
$$E_P = E_3 - \tfrac{1}{2}E_6$$
$$E_R = E_3 + E_1 - E_7$$

since the activation energy for photo-initiation can be taken as zero, we have

$$E_T - E_P = \tfrac{1}{2}E_1 = 7{\cdot}8 \text{ kcals.}; \text{ whence } E_1 = 15{\cdot}6 \text{ kcals.}$$

The determinations of the rates of initiation and chain lifetimes are not sufficiently accurate to enable precise values of E_2, E_4, and E_7 to be calculated, but it is clear that neither R_I nor τ is temperature dependent to more than a slight degree. The rates of initiation are consistent with a value of approx. 1 kcal. for E_I, which probably arises from the thermal contribution to R_I, and the same figure can be taken as an upper limit for E_4.

Hence, E_2 cannot be greater than 4·2 kcals. and E_7 is approximately zero, as would indeed be expected because the reaction of quinol with the peroxidic radicals must be an extremely facile process in order to replace the normal radical–radical termination of the uninhibited reaction.

Collected Kinetic Data.—From equations (4) and (5), since at 5° :

	Pure aldehyde.	30% Solution in decane.
R_L, mol./l.sec.	$(4{\cdot}54 \pm 0{\cdot}17) \times 10^{-4}$	$(2{\cdot}04 \pm 0{\cdot}08) \times 10^{-4}$
R_I, mol./l.sec.	$(1{\cdot}1 \pm 0{\cdot}1) \times 10^{-7}$	$(8{\cdot}1 \pm 0{\cdot}7) \times 10^{-8}$
[R·CHO], mol./l.	5·25	1·58
τ, sec.	$1{\cdot}1 \pm 0{\cdot}15$	$0{\cdot}6 \pm 0{\cdot}1$

therefore

k_2, mol.$^{-1}$/l.sec.	$(7{\cdot}2 \pm 1{\cdot}2) \times 10^{8}$	$(2{\cdot}7 \pm 0{\cdot}5) \times 10^{8}$
k_4, mol.$^{-1}$/l.sec.	$(7{\cdot}5 \pm 1{\cdot}2) \times 10^{6}$	$(3{\cdot}4 \pm 0{\cdot}8) \times 10^{7}$

These values of k_2 and k_4, although not affected in order of magnitude, do indicate that the *n*-decane has a slight influence on the reaction; hence in the following calculations the energies of activation are the only quantities which have been derived from the experiments conducted in solution.

It follows from equation (7) that, since at $[H_2Q] = 10^{-4}$ mol./l., $R_R = (2{\cdot}6 \pm 0{\cdot}1) \times 10^{-8}$ mol./l.sec., then

$$k_7 = \frac{k_2[\text{R·CHO}]R_I}{R_R[H_2Q]} = (1{\cdot}6 \pm 0{\cdot}3) \times 10^{3} \text{ mol./l.sec.}$$

Further, from the previous paper :

$$R_T = (k_1^{1/2}k_2/k_6^{1/2})[\text{R·CHO}]^{3/2}[O_2]^{1/2}$$

The oxygen term in this expression represents the concentration of oxygen in the liquid phase, and this may be estimated from the oxygen pressure if the absorption coefficient is taken to be 0·1 (Taylor and Hildebrand, *J. Amer. Chem. Soc.*, 1923, **45**, 682. Hence, since at 5° and 650 mm. of oxygen, $[O_2] = 3{\cdot}8 \times 10^{-3}$ mol./l. and $R_T = (1{\cdot}0 \pm 0{\cdot}2) \times 10^{-4}$ mol./l.sec., therefore $k_1 = (2{\cdot}6 \pm 0{\cdot}7) \times 10^{-7}$ mol./l.sec.

Evaluation of the velocity constants k_2 and k_4, which characterise the reactions of the aldehydic radicals, cannot be made under the present conditions because the oxygen pressure cannot be lowered sufficiently without encountering the complication of inadequate supply of oxygen.

Since velocity constants may be separated into temperature-independent and temperature-dependent terms in the manner :

$$k = Ae^{-E/RT} = PZe^{-E/RT}$$

values of the frequency factors, A, can now be obtained. The steric factors, P, are calculated on the assumption that the number of bimolecular collisions occurring per second in a normal liquid is 10^{11}. Hence :

$k_1 = (2{\cdot}6 \pm 0{\cdot}7) \times 10^{-7}$ mol./l.sec.;	$E_1 = 15{\cdot}6 \pm 1{\cdot}0$ kcals.;	$A_1 = 4 \times 10^{5}$;	$P_1 = 10^{-6}$
$k_2 = (7{\cdot}2 \pm 1{\cdot}2) \times 10^{8}$,,	$E_2 = 4{\cdot}2 \pm 0{\cdot}6$,,	$A_2 = 2 \times 10^{8}$;	$P_2 = 10^{-3}$
$k_4 = (7{\cdot}5 \pm 1{\cdot}2) \times 10^{6}$,,	$E_4 \sim 1$,,	$A_4 \sim 10^{8}$;	$P_4 \sim 10^{-3}$
$k_7 = (1{\cdot}6 \pm 0{\cdot}3) \times 10^{3}$,,	$E_7 \sim 0$,,	$A_7 \sim 2 \times 10^{3}$;	$P_7 \sim 10^{-8}$

The knowledge of the four velocity constants enables further information concerning the thermal process to be derived. This is summarised in Table VII, along with the corresponding data for the photo-oxidation, all results referring to a temperature of 5°.

TABLE VII.

	Thermal process.	Photo-process.
Rate of initiation, mol./l.sec.	$4{\cdot}2 \times 10^{-9}$	$1{\cdot}1 \times 10^{-7}$
Chain length	24,000	4,000
Chain lifetime, secs.	5·6	1·1
Stationary radical concn., mol./l.	$2{\cdot}4 \times 10^{-3}$	$1{\cdot}2 \times 10^{-7}$

DISCUSSION.

It is interesting to compare the present results with those of other workers in the field of autoxidation reactions. Table VIII contains all the detailed kinetic data available concerning such systems. The tetralin measurements have been made by Bamford and Dewar (*Proc. Roy. Soc.*, 1949, *A*, **198**, 252) and those of the other unsaturated hydrocarbons by Bateman and Gee (*loc. cit.*). The velocity coefficients quoted in the table have been adjusted by means of the corresponding activation energies to correspond to 15° where necessary.

TABLE VIII.

Kinetic data for autoxidation processes.

	Propagation reaction.			Termination reaction.		
Material.	k_2 (mol./l.sec.).	E_2 (kcals.).	A_2.	k_6 (mol./l.sec.).	E_6 (kcals.).	A_6.
*cyclo*Hexene	0·65	9·5	10^7	$0·95 \times 10^8$	<2	10^8—10^9
Methyl*cyclo*hexene ...	1·10	8·5	—	$0·5 \times 10^8$	<2	10^8—10^9
Dihydromyrcene ...	0·40	9·0	10^7	$0·65 \times 10^8$	<2	10^8—10^9
Ethyl linoleate	6·8	7·0	10^6	$0·5 \times 10^8$	<2	10^8—10^9
Tetralin	10·2	4·5	10^4	$2·0 \times 10^7$	1	10^8
n-Decanal	$1·1 \times 10^3$	4·2	10^8	$7·5 \times 10^8$	<1	10^8

Certain points emerge from an examination of this information. Consider, first, the termination process involving the interaction of two peroxidic radicals. The activation energy in every case is very low, as would be expected for such a reaction. From the constancy of their k_6 values, Bateman and Gee concluded that the reactivity of peroxidic radicals is independent of the structure of the molecules from which they are derived. Although the results for tetralin and *n*-decanal are somewhat larger, the variations in k_6 are not very large and the corresponding frequency factors lie within much narrower limits than have been found for the radical–radical termination steps of polymerisation reactions, for which values as low as 10^4 have been encountered (Burnett, *Quart. Rev.*, 1950, IV, 292).

As would be expected from the readiness with which the autoxidation of *n*-decanal occurs even at low temperatures, the velocity constant for the rate-controlling propagation step has a much higher value than is observed with the other materials studied. Apart from the result for tetralin, which seems to be rather low, the frequency factors, A_2, correlate well with those of transfer reactions in polymerisation calculated by Gregg and Mayo (*Faraday Soc. Disc.*, 1947, **2**, 328) and those found by Steacie, Darwent, and Trost (*ibid.*, p. 79), for hydrogen-exchange reactions with paraffin hydrocarbons. Each of these processes involves the abstraction of a hydrogen atom from a molecule either by a free radical or by an atom.

From the data published by Bateman and Gee and by Bolland and ten Have for the autoxidation of ethyl linoleate, it is possible to calculate a velocity coefficient for the interaction of the peroxidic radical with quinol at 5° :

For ethyl linoleate, $k_7 = 7 \times 10^6$ mol./l.sec.

For *n*-decanaldehyde, $k_7 = 1·6 \times 10^5$ mol./l.sec.

Comparison of these results would indicate that the reactivity of peroxidic radicals may not be entirely independent of the nature of the molecules from which they are derived, although the structural influence is not very great.

The value of k_1 is of particular interest, if the proposed mechanism of reaction is indeed correct, for it represents the first known determination of the velocity coefficient for chain initiation by the direct attack of molecular oxygen. The corresponding frequency factor brings the process into line with radical–molecule reactions, a reasonable result in view of the nature of the oxygen molecule. It is the high energy of activation which accounts for the relative inefficiency of the thermal chain initiation.

As can be seen from Table VIII, the number of autoxidation reactions which have been subjected to detailed kinetic analysis is still very small, and further investigations are needed before it is possible to assess more accurately the factors which control the radical reactivities.

We thank the Anglo-Iranian Oil Co., Ltd., for supplies of *n*-decane, and one of us (H. R. C.) is indebted to D.S.I.R. for the award of a Maintenance Allowance.

CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM, 15.

[*Received, January 10th*, 1951.]

446. *Trimethylgallium. Part I. The Relative Stabilities of its Co-ordination Compounds with the Methyl Derivatives of Groups* VB *and* VIB, *and the Thermal Decomposition of Some Trimethylgallium–Amine Complexes.*

By G. E. Coates.

Co-ordination compounds of trimethylgallium with all the trimethyl derivatives of the Group VB elements from nitrogen to antimony have been prepared; trimethylbismuth does not react. The donor properties of the VB elements, as measured by the dissociation of these co-ordination compounds, diminish regularly in the sequence N > P > As > Sb > Bi. A similar series of compounds between trimethylgallium and the dimethyl derivatives of the Group VIB elements (from O to Te) has also been prepared; the variation of donor properties to trimethylgallium in this group is irregular, *viz.*, O > Se > S = Te. Towards trimethylaluminium the donor properties of the Group VIB elements diminish regularly from oxygen to tellurium. This contrast between trimethylgallium and trimethylaluminium, together with a review of the other co-ordination compounds of the Group VIB elements, suggests that double bonding by means of *d* orbitals plays an important part in determining the stability of the co-ordinate link. The co-ordinating properties of ethers are discussed, and some complexes between silver iodide and dimethyl selenide and telluride are described.

The elements of Group IIIB, *viz.*, boron, aluminium, gallium, indium, and thallium, show a remarkable variation in their electron-acceptor properties. Compounds of all these elements in their tervalent states tend to increase their covalency to four, or sometimes six, by co-ordination with donor molecules. Boron, aluminium, and gallium exhibit this tendency to such a degree that, in some of their compounds, the element contrives to increase its covalency above three without acquiring an electron from a donor molecule; these compounds are the well known "electron-deficient" molecules exemplified by diborane B_2H_6, trimethylaluminium Al_2Me_6, and digallane Ga_2H_6, in which the total number of valency electrons is less than twice the number of valency bonds (see Coates, *Quart. Reviews*, 1950, **4**, 217).

The co-ordination compounds of the trimethyl derivatives of these elements are particularly suitable for studies on relative electron-acceptor and -donor properties, since the trimethyl derivatives themselves are all conveniently volatile and stable, and it is frequently possible to investigate their dissociation equilibria in the gas phase. The co-ordination compounds of trimethylboron have been thoroughly examined by H. C. Brown and others, and Brown and Davidson (*J. Amer. Chem. Soc.*, 1942, **64**, 316) have studied some co-ordination compounds of trimethylaluminium (these results are reviewed by Sidgwick, "The Chemical Elements and their Compounds," Oxford, 1950). Compounds have been described between trimethylgallium and the donor molecules, ammonia and ethyl ether (Kraus and Toonder, *Proc. Nat. Acad. Sci.*, 1933, **19**, 292), trimethyl- and triethyl-amine (Wiberg, Johannsen, and Stecher, *Z. anorg. Chem.*, 1943, **251**, 114). The reactions between trimethylgallium and the methyl derivatives of the elements of Groups VB and VIB have now been studied with the object of determining the relative donor properties of these elements towards a common acceptor molecule, trimethylgallium, and of establishing the acceptor properties of the latter in relation to boron and aluminium. The methyl derivatives of the donor elements are suitable for this purpose, since there is no possibility of reaction (at the temperatures involved in this work, *viz.*, <200°) other than the formation of a co-ordination compound. Compounds containing hydrogen bonded to nitrogen or other donor atoms frequently co-ordinate to trimethylgallium and then undergo further reaction with elimination of methane. Some of these reactions, which also take place with trimethylboron and trimethylaluminium, are described.

Trimethylgallium forms 1 : 1 co-ordination compounds with the methyl derivatives of all the VB and VIB elements except bismuth; trimethylbismuth did not combine even in the liquid state, since the vapour pressure of an equimolar mixture of the components slightly exceeded that calculated for an ideal solution. The physical properties of all the other compounds are given in Table I, which also includes the compounds formed with dimethylamine,

methylamine, and ammonia. The compound, trimethylgallium–trimethylamine (Wiberg *et al.*, *loc. cit.*) is very stable, as judged by its rather high melting point, 96·2°, and the fact that it begins to show perceptible dissociation in the gas phase only above 110°. This compound, made during the present work, exhibited dimorphism; crystals condensed from the vapour above 18—20° were quite transparent, had very rounded edges, and an almost glassy appearance

TABLE I.

Co-ordination compounds of trimethylgallium.

Compound.	M. p.	B. p. (extrap.).	*A*.*	*B*.	L_V.†	Trouton const.	Temp. range.
$Me_3Ga\text{–}NMe_3$ [a] ...	96·2°	164°	2226	7·947	10·19	23·3	96—107°
$Me_3Ga\text{–}NHMe_2$ ...	33·3—33·6	170	2532	8·596	11·6	26·2	50—110
$Me_3Ga\text{–}NH_2Me$ ...	37—38	169	2760	9·119	12·6	28·6	50—120
$Me_3Ga\text{–}NH_3$ [b]	31—32	179	1947	7·190	8·9	19·7	20—70
$Me_3Ga\text{–}PMe_3$	56·4—56·7	173	2662	8·851	12·2	27·3	60—120
$Me_3Ga\text{–}AsMe_3$	23·4—23·7	121	2458	9·114	11·2	28·5	25—100
$Me_3Ga\text{–}SbMe_3$	0·3—2·2	95	2105	8·591	9·6	26·1	16—40
$Me_3Ga\text{–}OMe_2$	—	100	2078	8·453	9·5	25·5	20—60
$Me_3Ga\text{–}SMe_2$	—	116	2580	9·516	11·8	30·4	20—60
$Me_3Ga\text{–}SeMe_2$	−43° to −42°	111	2783	10·118	12·7	33·0	15—80
$Me_3Ga\text{–}TeMe_2$	−32·5° to −32°	122	2488	9·172	11·4	28·8	20—80
$(Me_3Al\text{–}SeMe_2$ [c] ...	—	146	2320	8·410	10·6	25·3	20—120)
$(Me_3Al\text{–}TeMe_2$ [c] ...	—	146	2022	7·708	9·3	22·1	20—120)

* $\log_{10}(\text{v. p.})_{mm.} = -(A/T) + B$. † Latent heat of evaporation, kcals./g.-mol.

[a] Data from Wiberg, Johannsen, and Stecher, *loc. cit.* [b] Kraus and Toonder, *loc. cit.*, give m. p. 31°. [c] These aluminium compounds are discussed later, but are included in this Table for convenience.

New compounds are listed only in this Table; they are not mentioned again in the Experimental section.

but, on cooling to 10° or below, they slowly changed to a polycrystalline opaque mass. This change is reversible. The vapour pressure at these temperatures is too small to allow the detection of any change of slope in the log v.p.–T^{-1} graph.

All these compounds, except trimethylgallium–ammonia, have unusually large Trouton constants, rising to the remarkable value 33 for the dimethyl selenide complex. Brown and Davidson (*loc. cit.*) record large Trouton constants for some of the corresponding trimethylaluminium compounds, *e.g.*, 27·2 for $Me_3Al\text{–}SMe_2$. In these instances high Trouton constants are probably largely caused by dipole association, since co-ordination compounds of this type generally have large dipole moments. For example, Laubengayer and Finlay (*J. Amer. Chem. Soc.*, **1943**, **65**, 884) report Trouton constants of 33·0 and 32·8 for $MeEtO\text{–}BF_3$ and $Et_2O\text{–}BF_3$ respectively (dipole moments 5·07 and 4·92 D.). The effect may in some cases be enhanced when the process of evaporation is accompanied by partial or complete dissociation of the complex. The compounds of trimethylgallium with the trimethyls of the VB elements from nitrogen to antimony must have a high degree of molecular symmetry (like hexamethylethane), and are all solid at room temperature with the exception of $Me_3Ga\text{–}SbMe_3$, which is the least stable, being wholly dissociated as vapour. Its melting range +0·3—2·2° may be caused by some dissociation in the liquid (a slight excess of the more volatile component, trimethylgallium, may be present in the vapour above the melting solid). The less symmetrical compounds with dimethyl ether, and dimethyl sulphide, selenide, and telluride are all liquids of fairly low freezing point.

With the exception of the compounds with dimethylamine, methylamine, and ammonia,

which decompose when heated (see below), relative stabilities were determined by dissociation measurements in the vapour phase. Heats of dissociation, derived from the slope of the log K_p (dissociation constant)–T^{-1} graph, were also measured in favourable cases; when the dissociation is of the order of 90% or more the values for ΔH are only approximate. The uncertainty in ΔH is probably about ± 1 kcal./g.-mol. in the case of $Me_3\bar{G}a\text{–}\dot{P}Me_3$ and rather greater for the others; the order of stability is more reliable. These measurements are summarised in Table II.

TABLE II.

Relative stability of the co-ordination compounds of trimethylgallium.

Donor molecule.	Dissociation (100°), %.	K_p (atm.) at 100°.†	$-\Delta H$.*
NMe_3	~0	Very small	—
PMe_3	<10 (22% at 130°)	0·03 (at 130°)	18
$AsMe_3$	75	1·34	10
$SbMe_3$	100	(∞)	—
$BiMe_3$	No compound formed even in liquid.		
OMe_2	70	1·07	9·3
SMe_2	~90	~2·5	~8
$SeMe_2$	78	1·52	10
$TeMe_2$	~90	~2·5	~8

* Heat of dissociation, kcals./g.-mol. † Dissociation constant.

The order of decreasing donor properties, from Table II, is:

Group VB: >N >P >As >Sb >Bi

Group VIB: >O >Se >S = Te

Relative Acceptor Properties: Group IIIB.—These results, in addition to showing the relative donor properties of the methyls of the VB and VIB elements, which are further discussed below, enable the acceptor properties of trimethylgallium to be compared with those of trimethylboron and trimethylaluminium. Trimethylboron–trimethylamine is 92% dissociated at 100° (Brown and Gerstein, *ibid.*, 1950, **72**, 2923), and trimethylboron forms a compound with trimethylphosphine of as yet unknown heat of dissociation (Brown and Harris, *ibid.*, 1949, **71**, 2751). Trimethylboron does not react with dialkyl ethers. Brown and Davidson (*loc. cit.*) obtained an order of stability N > P > O > S for the corresponding compounds of trimethylaluminium (other donor elements were not investigated, but methyl chloride did not react), all of which are much more stable than their gallium analogues. Hence trimethylgallium, though a stronger acceptor than trimethylboron, is weaker than trimethylaluminium. Trimethylindium is evidently practically devoid of acceptor properties since it forms no ammines or ether complexes even at −35° (Dennis, Work, and Rochow, *J. Amer. Chem. Soc.*, 1934, **56**, 1047), while trimethylthallium may be separated from its very unstable ether complex $Me_3\bar{T}l\text{–}\dot{O}Et_2$ by distillation under reduced pressure (Gilman and Jones, *ibid.*, 1946, **68**, 517). Thus, in the absence of any quantitative measurements on indium and thallium alkyls, the relative acceptor properties of the trimethyls of the Group IIIB elements may provisionally be written:

$$Al > Ga\ (>Tl?) > B > In.$$

The position of aluminium at the head of this somewhat irregular series is in agreement with the fact that only trimethylaluminium is dimeric in the vapour phase [trimethylthallium (*idem, ibid.*), which is liable to explode on heating, is monomeric in benzene solution]. Only in aluminium is the tendency to form four covalent bonds sufficiently strong to stabilise the type of electron-deficient ring structure probably present in Al_2Me_6; the hydrides of boron and gallium are, however, dimeric (B_2H_6, Ga_2H_6), while aluminium hydride is polymeric $(AlH_3)_n$.

The high stability of the trimethylaluminium compounds investigated by Davidson and Brown (*loc. cit.*) prevented the measurement of heats of dissociation, except in the case of the dimethyl sulphide complex $Me_3\bar{A}l\text{–}\dot{S}Me_2$ ($\Delta H = -19 \pm 2$ kcals./g.-mol., 27% dissociated at 100°). The comparative stabilities of the other compounds with NMe_3, PMe_3, and Me_2O, which did

not dissociate perceptibly in the temperature range investigated, were determined by displacement reactions. Trimethylaluminium–trimethylphosphine ($Me_3\overset{-}{A}l\text{–}\overset{+}{P}Me_3$) gave trimethylaluminium–trimethylamine ($Me_3\overset{-}{A}l\text{–}\overset{+}{N}Me_3$) and trimethylphosphine quantitatively when heated with trimethylamine, showing that trimethylamine is a stronger donor molecule than trimethylphosphine. In the present work trimethylphosphine similarly displaced trimethylarsine quantitatively from its trimethylgallium complex, and trimethylamine quantitatively displaced trimethylphosphine:

$$Me_3\overset{-}{G}a\text{–}\overset{+}{A}sMe_3 + PMe_3 \longrightarrow Me_3\overset{-}{G}a\text{–}\overset{+}{P}Me_3 + AsMe_3$$

and

$$Me_3\overset{-}{G}a\text{–}\overset{+}{P}Me_3 + NMe_3 \longrightarrow Me_3\overset{-}{G}a\text{–}\overset{+}{N}Me_3 + PMe_3$$

Similarly, as expected, trimethylamine displaced trimethylarsine. This method of investigating comparative stabilities is not suitable when the dissociation of the complex is appreciable at or a little below room temperature. For example, when trimethylgallium–trimethylarsine was heated with one molar equivalent of methyl ether (which forms a more stable complex, see Table II), until all was gaseous, the mixture then being cooled and subjected to fractional condensation, methyl ether was recovered quantitatively. In this instance methyl ether was by far the most volatile component present and its removal from the mixture by fractional condensation doubtless resulted in a displacement of the equilibrium:

$$Me_3\overset{-}{G}a\text{–}\overset{+}{A}sMe_3 + OMe_2\uparrow \rightleftharpoons Me_3\overset{-}{G}a\text{–}\overset{+}{O}Me_2 + AsMe_3$$

Relative Donor Properties: Group VB.—Towards a constant acceptor molecule, trimethylgallium, the donor properties of the Group VB trimethyls diminish steadily from nitrogen to bismuth. Since the formation of a co-ordination compound by a donor molecule consists essentially of the process, $Me_3M \longrightarrow Me_3\overset{+}{M}^- + e^-$, relative donor properties should be directly related to the first ionisation potentials, which are not known for the methyl derivatives concerned here. Three types of reaction may, however, be compared with the formation of a co-ordination compound. These are: (*a*) Reaction as a base, $Me_3M + HX \rightleftharpoons Me_3HM^+ + X^-$. Only the amines and the much weaker trialkylphosphines are basic in this direct sense, so the comparison cannot be carried far. (*b*) Reaction with methyl iodide, $Me_3M + MeI = Me_4M^+ + I^-$. Here it may be noted that trimethylbismuth alone of the series does not form a quaternary compound with methyl iodide. The comparative stabilities of the others are not known quantitatively; the greater *rate* of reaction of trimethylphosphine than of trimethylamine (Davies and Evans, *J.*, 1934, 244) is probably due to differences in the degree of steric hindrance since the C–N–C angle in NMe_3 (108° ± 4°; Brockway and Jenkins, *J. Amer. Chem. Soc.*, 1936, **58**, 2036) is greater than the C–P–C angle in PMe_3 (100° ± 4°; Springall and Brockway, *ibid.*, 1938, **60**, 996). (*c*) Reaction with oxygen, $2Me_3M + O_2 = 2Me_3\overset{+}{M}\text{–}\overset{-}{O}$. Here there is an apparent discrepancy, in the contrast between the difficulty of oxidation of trimethylamine, which requires hydrogen peroxide, and the extreme ease of oxidation (sometimes amounting to spontaneous inflammability) of all the other members of the series. This, however, is almost certainly due to the possibility of quinquevalency in all the elements except nitrogen. The trialkyl oxides, except $R_3\overset{+}{N}\text{–}\overset{-}{O}$, are probably mesomeric between $R_3\overset{+}{M}\text{–}\overset{-}{O}$ and $R_3M{=}O$, in which case the very easy reaction with molecular oxygen would proceed through the formation of an intermediate compound, for example:

$$Me_3M + O_2 \longrightarrow Me_3M{=}\overset{+}{O}\text{–}\overset{-}{O} \xrightarrow{Me_3M} 2Me_3M{=}O$$

(M = P, As, Sb, Bi, but *not* N.)

Reaction with a suitable acceptor molecule such as the trialkyls of some of the Group III elements appears to be the most reliable way of investigating relative donor properties. Stability comparisons, with transition metal halides as acceptor molecules, are complicated by the influence of solubility, since in a competition (or displacement) reaction between two donor molecules for a given acceptor the least soluble co-ordination compound is likely to separate irrespective of relative stabilities unless the equilibrium is very strongly in favour of the more soluble compound. However, the steady gradation in donor properties from nitrogen to

bismuth found in the present work is entirely in agreement with the known properties of transition-metal and other co-ordination compounds. Nitrogen (tervalent) forms complexes with a very large number of salts, and is generally regarded as the strongest donor atom. Phosphorus, in the alkyl- and aryl-phosphines, combines with many of the transition metals, also with the Group IB and IIB elements. Similar arsenic compounds combine with the same elements, but it may be significant that fewer of these compounds have been described, while antimony and bismuth act as donor atoms only to very powerful acceptors such as platinum and palladium. It is important that the donor properties of these elements are greatly influenced by the groups to which they are attached.* While ammonia forms so many metal complexes, triphenylamine does not combine even with platinum. The apparently more powerful donor properties of the trialkyl- and triaryl-phosphines and -arsines would seem to be in disagreement with the above generalisation. This is to be attributed to the possibility of π-bonding between donor and acceptor in the case of complexes between donor elements with vacant low-energy *d* orbitals (*i.e.*, excluding nitrogen) and transition elements with *d* orbitals which are partly or just completely filled, as suggested by Chatt (*J.*, 1949, 3340; 1950, 2301; *Nature*, 1950, **165**, 637). This aspect is more fully discussed in the next section.

Relative Donor Properties: Group VIB.—To trimethylgallium dimethyl ether, sulphide, selenide, and telluride are much weaker donors than trialkylamines or trialkylphosphines. The order within the group is rather peculiar, O > Se > S = Te. Again, the ionisation potentials of these compounds are not known, but applying the comparisons made in the previous section, it is found that: (*a*) Only the ethers show any basic properties, in accordance with the position of oxygen at the head of the donor series given above.

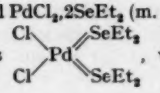
(*b*) In contrast to the ethers, dialkyl sulphides, selenides, and tellurides readily combine with methyl iodide, forming stable 'onium salts. The only known trialkyloxonium salts have to be prepared by other means; they are highly reactive, alkylating agents, and usually unstable to heat.

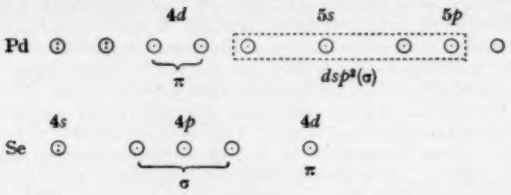
(*c*) Doubtless for the same reasons as apply to Group VB, the sulphides, selenides, and tellurides are readily oxidised; indeed, the ease of oxidation increases with atomic weight.

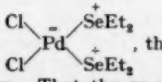
There are two striking features in the above order, (1) that selenium appears out of place, (2) that oxygen heads the order. It is difficult to comment on the former in relation to the known co-ordination compounds of this group, since there is no information allowing a comparison between the stabilities of the complexes formed by sulphides, selenides, and tellurides. The position of oxygen merits some consideration. With boron, aluminium, gallium, and possibly tin and titanium, oxygen co-ordinates more readily than sulphur (there is practically no information about selenium and tellurium in relation to some of these acceptor atoms other than that contained in this work). On the other hand, whereas sulphides, selenides, and tellurides co-ordinate with mercuric, palladous, and platinous halides, ethers do not. Considering how oxygen differs from the other elements of its group one finds (i) that its electronegativity is larger than that of any of the other donor atoms under discussion, and (ii) having no stable *d* orbital it cannot form double bonds of the type $R_2O{=}O$, unlike, for example, $R_2Se{=}O$.

With regard to (i), in the trialkyloxonium salts, which are less stable than the 'onium salts of sulphur, selenium, and tellurium, a formal positive charge is imposed on the oxygen atom. This is doubtless reduced somewhat by polarisation of the three C–O bonds in the sense $\overset{\delta+}{C}{-}\overset{\delta-}{O}$, but a positive charge on a highly electronegative atom is likely to cause some instability. In its co-ordination complexes, on the other hand, the oxygen atom may be held to the acceptor atom by electrostatic attraction between the negatively charged lone pairs of the oxygen and the positive centre of the acceptor. This would be the type of bonding described by Lennard-Jones and Pople (*Proc. Roy. Soc.*, 1951, *A*, **205**, 155) in their discussion of hydrogen bonding, the formation of many salt hydrates, and some co-ordination compounds. It is possible that the co-ordination compounds of oxygen differ from those of other donor atoms in that their bonding is predominantly electrostatic in nature rather than covalent. With regard to the covalency limit of three [see (ii) above], one finds that all the stable complexes containing sulphur, selenium, or tellurium as donor atoms involve acceptor atoms with incomplete or just completed *d* groups, *e.g.*, palladium, silver, and mercury; in all these instances no corresponding oxygen compounds have been described. It seems very likely that the former have not the true co-ordination structure, but are mesomeric between the latter and a formulation in which the donor atom is bound to the metal by a double bond, for which the *d* orbital of the metal

* The author is indebted to a Referee for drawing his attention to this point.

contributes the π-component. For example, the compound $PdCl_2,2SeEt_2$ (m. p. 45°; Fritzmann, *Z. anorg. Chem.*, 1924, **133**, 119) may be formulated as  , with the following atomic orbital configurations :



In this formulation, in contrast to the true co-ordination structure,  , the electropositive metal atom is not loaded with a double negative charge. That the co-ordination structure of these compounds contributes largely to the mesomeric form follows from the high diple moments of their *cis*-forms (for examples see "Tables of Electric Dipole Moments," L. G. Wesson, Massachusetts Inst. Technology, 1948; the moment of the compound quoted is not known, but that of the *cis*-form of its platinum analogue is 9·1 D.). The non-combination of ethers with such strong acceptor molecules as the halides of palladium, platinum, and mercury may thus be due in part to the impossibility of this type of mesomeric stabilisation when oxygen is the donor atom. This type of stabilisation will be more pronounced, the greater the tendency of the donor atom to assume a quadricovalent configuration. This tendency, judged by the relative ease of oxidation of sulphides, selenides, and tellurides, increases with atomic weight in that order. It is not therefore surprising to find that the stability of the complexes between mercuric halides and dimethyl sulphide, selenide, and telluride increases in the order, S, Se, Te, the evidence for this being the relative ease with which the complexes lose the donor molecule when heated or exposed to the air (Coates and Miss V. Hodson, unpublished observations). Similarly, two compounds $AgI(TeMe_2)_2$ and $(AgI)_2TeMe_2$ have been isolated by the addition of an acetone solution of dimethyl telluride to a solution of silver iodide in concentrated aqueous potassium iodide; these are unstable and smell strongly of dimethyl telluride. Dimethyl selenide gives a colourless compound $(AgI)_2SeMe_2$, which is so unstable that it quickly shows the yellow colour of silver iodide when exposed to air, while dimethyl sulphide and diethyl ether show no sign of combining with a solution of silver iodide.

The increase in the stability of trimethylgallium co-ordination compounds as one passes from dimethyl sulphide to dimethyl selenide may be explained in a similar way, *viz.*, by the increased mesomeric contribution of the double bonded structure (*b*) :

(*a*.) $Me_3Ga\overset{-}{-}\overset{+}{S}eMe_2$ $\qquad\qquad$ $Me_3Ga{=}SeMe_2$ (*b*.)

The electronic configuration of the gallium atom in structure (*b*) is :

The donor properties of the Group VIB elements, *i.e.*, the tendency to form true co-ordination compounds with the structure of type (*a*), diminish with increasing atomic weight. This is evident from their behaviour, described below, towards trimethylaluminium, and also by analogy with Group VB elements. It is suggested that the ability of the Group VIB elements to form double-bonded structures of type (*b*) increases with atomic weight. Since the stability of the mesomer must depend on a balance between both these tendencies, the irregularity O > Se > S = Te in the observed stability series may be at least qualitatively accounted for.

These suggestions can be tested by reference to aluminium which, having no *d* group, cannot form (*b*)-type double-bonded structures. In contrast to trimethylgallium, trimethylaluminium should form a *weaker* compound with dimethyl selenide than with dimethyl sulphide and a still

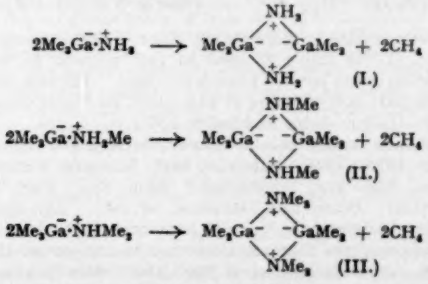
weaker compound with dimethyl telluride. The compound trimethylaluminium–dimethyl selenide (which was not mentioned by Brown and Davidson, *loc. cit.*) was therefore prepared and its stability measured by gas-phase dissociation; from the slope of the $\log_{10} K_p$–T^{-1} graph, ΔH, the heat of the reaction $Me_3\bar{A}l\text{–}\overset{+}{S}eMe_2 \rightleftharpoons \frac{1}{2}Me_6Al_2 + SeMe_2$, is 6 kcals./g.-mol. Since the heat of the reaction $\frac{1}{2}Me_6Al_2 \rightleftharpoons Me_3Al$, $\Delta H'$, is $-10{\cdot}1$ kcals./g.-mol. (Laubengayer and Gilliam, *J. Amer. Chem. Soc.*, 1941, **63**, 477), the heat of the dissociation $Me_3\bar{A}l\text{–}\overset{+}{S}eMe_2 \rightleftharpoons Me_3Al + SeMe_2$ is 16 kcals./g.-mol. The compound is 40% dissociated at 100° and 54% at 130°, whereas Brown and Davidson found that the heat of dissociation of $Me_3\bar{A}l\text{–}\overset{+}{S}Me_2$ is 19 kcals./g.-mol. and the extent of dissociation is 27% at 100°. Trimethylaluminium–dimethyl telluride was also prepared; its dissociation in the temperature range 100—150° was so great (approaching 100% at 140°) that the heat of dissociation could not be measured. The vapour-pressure constants of these compounds are given in Table I. It is clear that to aluminium, with no possibility of double bonding by means of a *d* orbital, the donor properties of the Group VIB elements decrease with increasing atomic weight in the normal way, O > S > Se > Te.

It is, of course, probable that the co-ordination compounds of the Group VB elements with acceptor atoms with suitable *d* orbitals are also stabilised by partial double bonding. In this series, however, as far as gallium is concerned, any such effect would appear to be subordinated to the decrease of true donor tendency with increasing atomic weight. That some double bonding by *d* orbitals contributes to the structure of various platinum compounds with phosphines and with olefins has already been indicated by Chatt (*loc. cit.*). The dipole moments of the *cis*-series of complexes between platinous chloride and trimethyl-phosphine, -arsine, and -stibine decrease in the order 10·7, 10·5, 9·2 (Jensen, *Z. anorg. Chem.*, 1936, **229**, 225), although the lengths of the co-ordinate bonds must increase with the atomic weight of the donor atom. It is probable that increasing contribution of type-(*b*) double-bonded structures more than offsets the increase of bond length and causes the net decrease of dipole moment.

The relative importance of π-bonding by *d* orbitals is clearly much greater with platinum than with gallium, since Chatt (*J.*, 1951, 652) has recently shown that the co-ordinating affinity of the *n*-propyl derivatives of the Group VB elements towards platinous chloride is in the order P > As > Sb > N > Bi. The possible stabilisation of co-ordination compounds by mesomerism involving VB elements in the quinquecovalent state is at present being studied in this laboratory.

In general, it would appear very likely that mesomerism between the true co-ordination structure $\bar{A}\text{–}\overset{+}{B}$ and the double-bonded structure A=B (involving *d* orbitals in the π-component) plays an important part in stabilising all co-ordination compounds in which the donor and acceptor atoms have appropriate *d* groups.

Decomposition of the Compounds between Trimethylgallium and Ammonia, Methylamine, and Dimethylamine.—Each of these compounds decomposed when heated, with the loss of one molecule of methane per gallium atom. The products are dimeric in the gas phase and probably have the four-membered ring structure * already assigned to some similar compounds of boron and aluminium (*e.g.*, Brown and Davidson, *loc. cit.*).



Some properties of these compounds are given in Table III.

* The names, (I) *cyclo*(bisammonium bisdimethylgallide), (II) *cyclo*(bismethylammonium bisdimethylgallide), and (III) *cyclo*(bisdimethylammonium bisdimethylgallide), are tentatively suggested for this novel type of compound. ED.

TABLE III.

Associated condensation compounds derived from trimethylgallium.

Compound.	M. p.	B. p. (extrap.).	*A*.*	*B*.*	L_v.†	Trouton const.	Temp. range.
(III)	—	—	1450	4·850	6·63 ‡	—	30— 55°
(III)	—	—	2712	12·652	12·46 ‡	—	80—150
(II)	—	—	2666	8·656	12·2	—	30— 90
(II)	—	226°	2078	7·045	9·5	19·1	90—140
(I)	97·2—97·5°	—	3940	11·72	18·0 ‡	—	50— 90
(I)	—	212	2800	8·648	12·8	26·4	100—140

* Log_{10} (v. p.)$_{mm.} = -(A/T) + B$. † Latent heat of evaporation, kcals./g.-mol.
‡ Latent heat of sublimation.

FIG. 1.

Vapour pressure of $(Me_2Ga{-}NHMe)_2$ (II), *liquid.*

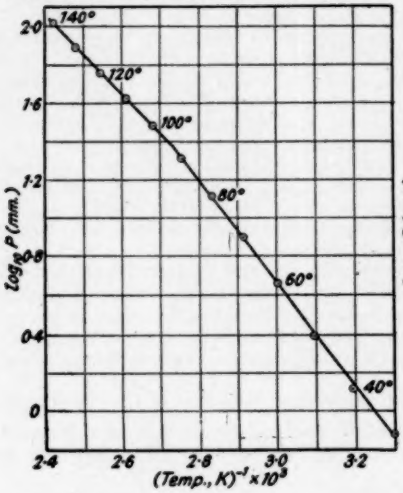
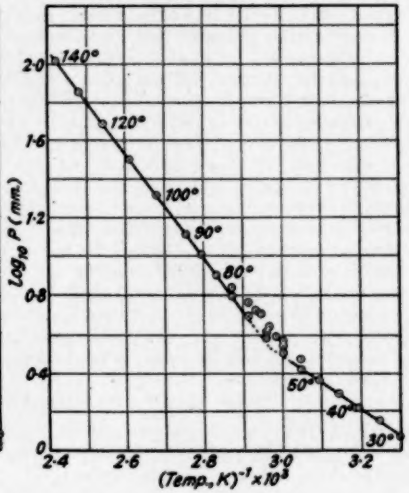


FIG. 2.

Vapour pressure of $(Me_2Ga{-}NMe_2)_2$ (III), *solid.*



Trimethylgallium–ammonia begins to evolve methane at 70° and decomposes into (I) and methane quite rapidly at 90°. On further heating above 140° (I) begins to form more methane and a white non-volatile substance of amorphous appearance, almost certainly polymeric :

$$(Me_2Ga{-}NH_2)_2 \xrightarrow{>140°} [\cdot MeGa{-}NH\cdot]_n + CH_4$$

Trimethylgallium–methylamine is more stable, since it begins to split off methane only at 120—130°. The product (II) is stable at least to 180° without further methane evolution, although one hydrogen atom is still bonded to each nitrogen. Trimethylgallium–dimethylamine begins to decompose into (III) and methane at 115—130°, so it is of comparable stability to the methylamine compound; (III) is stable at least to 180°.

Similar compounds of boron and aluminium have been described [boron : Wiberg, " F.I.A.T. review of German Science, 1939—1946," published 1949, Inorganic Chemistry, Part I, pp. 129—137; Goubeau, *ibid.*, pp. 228—234; aluminium : Bähr, *ibid.*, Part II, pp. 159—160; the aluminium analogue of (III) : Brown and Davidson, *loc. cit.*]. The loss of methane from the co-ordination compounds of trimethylboron with ammonia, methylamine, and dimethylamine requires much higher temperatures than are necessary to decompose those of aluminium and gallium. The boron compounds decompose at 280—330°, while those of aluminium appear to be somewhat less stable than their gallium analogues, their decomposition temperatures being 57—70° (NH_3), 55—57° (NH_2Me), and 90—120° ($NHMe_2$), in contrast to 70°, 120—130°, and 115—130°. The molecular weights of the boron analogues of (I) and (II) indicate a reversible equilibrium between the mono- and di-meric (ring) forms, while $Me_2B{-}NMe_2$ is monomeric

(Goubeau, *loc. cit.*; Coates, *J.*, 1950, 3481). Like (I), $Me_2Al{-}NH_2$ (m. p. 134·2°) was found to be dimeric (cryoscopically in liquid ammonia). The aluminium analogue of (III), *viz.*, $Me_2Al{\cdot}NHMe$, is much less stable than (II), since it loses methane even at its melting point ~110°, giving a polymeric product, and its molecular complexity was not determined.

Some of the physical properties of compounds (II) and (III) are rather peculiar. The vapour pressures of these compounds are plotted in Figs. 1 and 2; (II) shows a discontinuity at 90°, latent heats of evaporation above and below this temperature being 9·5 and 12·2 kcals./g.-mol. respectively, with, however, no apparent phase change since the compound is liquid throughout the measured temperature range 30—140°. The latent heat from 90° to 140° is unusually low for this class of compound, the Trouton constants of which are generally rather high. The compound (III) derived from dimethylamine is solid at least up to 150° and appears to have a remarkably low latent heat of sublimation from 30° to about 55°, *viz.*, 6·6 kcals./g.-mol. Between 55° and 80° the vapour pressure was erratic and the various points in Fig. 2 shown for this region were obtained in several independent experiments. The remainder of the graph was reproducible. In the 55—80° range the higher vapour pressures were obtained on cooling from a higher temperature, and the lower points on heating. The most extraordinary feature is the apparent *increase* of latent heat of sublimation in this temperature range, amounting to 5·9 kcals./g.-mol., which suggests that the high-temperature form has a lower energy than the low-temperature form. Crystals condensing at or near room temperature are very well formed, with sharply defined faces and angles, but those condensing above about 80° are of dendritic habit, with a strong tendency to form rounded edges. It is possible that the low- and high-temperature forms differ in chemical bonding, *e.g.*, the former might be a molecular crystal consisting of four-membered cyclic molecules, while the latter might perhaps have a linear polymeric structure:

Experimental.

All the compounds described were prepared and studied in a vacuum apparatus of the type described by Stock ("The Hydrides of Boron and Silicon," Cornell, 1933) and by Sanderson ("The Vacuum Manipulation of Volatile Compounds," Wiley, 1948). In general, weighed quantities of the two components were condensed in the "high-temperature bulb" (Burg and Schlesinger, *J. Amer. Chem. Soc.*, 1937, **59**, 780; Sanderson, *op. cit.*), and vapour pressures and thermal dissociations were measured in this. All the compounds were sufficiently volatile at room temperature to allow of their weights being checked directly after these measurements. The methane evolved in the decomposition of compounds containing active hydrogen was identified by its vapour pressure at −183° and transferred to a gas burette by a Töpler pump.

Preparation of Materials.—Trimethylgallium was prepared by a modification of Wiberg, Johannsen, and Stecher's method (*Z. anorg. Chem.*, 1943, **251**, 114). Metallic gallium (6·75 g.) and dimethylmercury (37 g.), with a trace of mercuric chloride, were heated to boiling in a bulb sealed to a 20-cm. fractionating column packed with Fenske helices, in an atmosphere of dry nitrogen (1 atm. pressure). After 2 hours the temperature of reflux at the top of the column began to fall from 92° (b. p. of $HgMe_2$), and after 5 hours became steady at 55—56° (b. p. of $GaMe_3$). From time to time during the next 3 days small amounts of pure trimethylgallium were taken off from the top of the column until a residue of mercury and about 1 c.c. of liquid, consisting mainly of trimethylgallium, were left. The conversion was virtually complete and no decomposition occurred. The distillate of trimethylgallium was frozen and transferred in a nitrogen atmosphere to the vacuum apparatus, where it was stored under its own vapour pressure.

Trimethylamine was purified by treatment with phosphoric anhydride, which removes primary and secondary amines (Brown, Taylor, and Gerstein, *J. Amer. Chem. Soc.*, 1944, **66**, 431); dimethylamine was prepared from *N*-nitrosodimethylamine and dried by shaking with a liquid sodium–potassium alloy. Methylamine was purified by boiling a 90% neutralised solution, which expels practically all ammonia present, followed by recrystallisation of the picrate. The free base was then dried with potassium, which dissolves to give a blue solution in the anhydrous amine, followed by fractional distillation in a 30-cm. low-temperature fractionating column. Ammonia from a cylinder was dried by sodium and used without further purification.

Trimethylphosphine was obtained by the action of methylmagnesium iodide on phosphorus trichloride; it was separated as the silver iodide complex $(Me_3P,AgI)_4$, which was dried and heated in a vacuum, giving pure trimethylphosphine (Mann and Wells, *J.*, 1938, 702). Trimethylarsine was prepared similarly by thermal decomposition in a vacuum of the palladium compound $(Me_3As)_2PdCl_2$ (*idem, ibid.*). Trimethyl-stibine and -bismuth were prepared by the Grignard reaction from the chlorides, and were purified by fractionation in a nitrogen atmosphere at low pressure in the vacuum apparatus.

Methyl ether, from sodium methoxide and methyl iodide in methanol, was purified by means of the low-temperature fractionating column. Methyl sulphide was purified by fractionation of the commercial

product. Methyl selenide, prepared by the method of Bird and Challenger (*J.*, 1942, 570), and methyl telluride (*idem*, *ibid.*, 1939, 166) were purified by fractionation in the vacuum apparatus.

Analysis.—The compounds described were not subjected to analysis, since they were all prepared in the vacuum apparatus from materials of known purity, and as nothing is lost by this (quantitative) technique, the method of preparation itself constitutes an analysis. In decompositions involving the formation of methane, the latter was always measured in a gas burette.

Fractionation in the vacuum apparatus by the method of fractional condensation was greatly facilitated by use of the unit shown in Fig. 3. The substance was evaporated from the bulb and was condensed in the low-temperature bath at the top of the column held at such a temperature that the gas pressure was 1—2 mm. Fractionation took place in the vacuum-jacketed column packing (Fenske helices); gas was slowly taken off from the top, and either transferred directly to a vapour-pressure bulb or passed through the usual set of three or four fractional condensation U-tubes.

FIG. 3.

To illustrate the experimental methods used, the preparation of two compounds is described, *viz.*, trimethylgallium–dimethyl ether and the compound $(Me_2Ga{-}NMe_2)_x$ obtained by heating trimethyl-gallium–dimethylamine.

Trimethylgallium–Dimethyl Ether.—20·4N-c.c. (*i.e.*, c.c. at N.T.P.) of methyl ether (0·911 millimol.) were measured at a pressure of 47 mm. in a gas-volume-measuring apparatus (see Sanderson, *op. cit.*) and transferred to the high-temperature bulb (164-c.c. volume); the same volume of trimethylgallium was measured and condensed in the same high-temperature bulb. These two components were isolated from the remainder of the apparatus by raising mercury in the manometer tube which formed the connection between the high-temperature bulb and the vacuum apparatus, and the contents of the bulb were allowed to warm to room temperature. The bulb was then surrounded by an oil-bath (thermostat), and vapour pressures were measured at 5° intervals. When the compound was entirely gaseous (65°), the temperature was raised a further 10° and then pressures were measured at 5° intervals up to 120°, a similar series of pressures being measured at decreasing temperatures. From the known volume, temperature, and pressure, the total number of moles of gas was obtained. From this and the number of moles (0·911) of complex introduced into the bulb, the amount of dissociation and the equilibrium constant (K_p) were calculated for each temperature. The slope of the log K_p–T^{-1} plot gave the heat of dissociation. After the experiment the compound was transferred to a weighing tube, attached to the vacuum apparatus by a ground joint and in which the greased tap could be protected from the vapour of the compound by a mercury seal (Stock, Sanderson, *opp. cit.*), and weighed (145·9 mg.; 0·911 millimol. = 146·6 mg.). Its composition is thus settled.

cyclo-(1 : 3-*Bisdimethylammonium* 2 : 4-*Bisdimethylgallide*).—Trimethylgallium (0·3662 g.), equivalent to 71·5N-c.c., was transferred to the high-temperature bulb and kept at −183° while 71·5N-c.c. of dimethylamine were measured by volume and condensed on the trimethylgallium. On warming to room temperature the mixture partly melted and then solidified. When the high-temperature bulb was heated in the thermostat for vapour-pressure measurements, the solid *compound* was observed to melt over the range 33·3—33·6° and then pressures were measured up to 110°. Above this temperature the pressure slowly increased when the temperature was held constant. The bulb was then heated to 170° and kept at that temperature until no further pressure change occurred. On cooling, white crystals were deposited on the walls of the bulb. The pressure was 83 mm. when the bulb was cooled in liquid oxygen (v. p. of methane = 81·1 mm. at −183°), showing that the gas present was methane. The latter was pumped into the gas burette by means of a Töpler pump and measured 71·2N-c.c.; thus one mole of methane was formed from one mole of trimethylgallium; the residue therefore had the composition $(Me_2Ga{\cdot}NMe_2)_x$. After removal of the methane the vapour pressure of the residue was determined, followed by measurements of temperature and pressure when all the solid had vaporised. From the latter the volume corresponded to 35·7 c.c. at 170°, 35·8 at 175°, and 35·8 at 180° (Calc. for $x = 2$, 35·75 c.c.).

These methods were used to prepare and characterise the *compounds* listed in Tables I and III.

Some Co-ordination Compounds of Dimethyl Telluride.—Silver iodide–bis(dimethyl telluride). Dimethyl telluride (3·05 g., 0·02 mol.) in acetone (20 c.c.) was added to a solution of silver iodide (2·35 g., 0·01 mol.) in nearly saturated aqueous potassium iodide (10 c.c.). A white precipitate appeared which dissolved on warming; on cooling, the long colourless needles (4·2 g., 78%) which separated were collected and washed with a little acetone. Recrystallisation from acetone was accompanied by some decomposition and deposition of a little white insoluble matter which was removed before crystallisation of the product, m. p. 73—74° (corr.) with softening at 60—62° (sealed m. p. tube). The product, which smells strongly of dimethyl telluride, loses the latter quantitatively when heated in a vacuum at 180° (yellow silver iodide begins to appear at 90°); it was analysed by means of this decomposition, 0·1744 g. giving 0·0778 g. of silver iodide (completely soluble in concentrated aqueous potassium iodide). Thus the compound contained 20·4% of silver [$AgI(TeMe_2)_2$ requires Ag, 19·6%]. A somewhat high silver content would be expected since the compound so easily loses dimethyl telluride. An acetone solution gives a heavy yellow precipitate of silver iodide with a solution of silver nitrate; this points to a constitution $[Me_2Te{\rightarrow}Ag{\leftarrow}TeMe_2]^+ I^-$.

Dimethyl telluride–bis(silver iodide). Dimethyl telluride (6·1 g., 0·04 mol.) in acetone (35 c.c.) was added to a solution of silver iodide (18·8 g., 0·08 mol.) in concentrated aqueous potassium iodide (80 c.c.). A white precipitate appeared together with a heavy yellowish oil. When heated for a short time the

oil dissolved and a thick white precipitate appeared. This was collected and washed with acetone, concentrated aqueous potassium iodide, and finally acetone. This product (22 g., 88%) was insoluble in water, alcohol, acetone, or benzene; when it was heated with alcohol or benzene, the yellow colour of silver iodide appeared, but vanished again on cooling. It melted at 137—138° (corr., sealed tube) with decomposition to a black liquid [Found : Ag, 34·3%, by conversion into silver iodide by 1 hour's heating at 180° in high vacuum. $TeMe_2(AgI)_2$ requires Ag, 34·4%].

Dimethyl Selenide–Bis(silver Iodide).—Dimethyl selenide (3 c.c., slightly more than one molar equivalent) in acetone (20 c.c.) was added to silver iodide (8·5 g.) in saturated aqueous potassium iodide (15 c.c.). Distilled water was added gradually to the warmed solution until precipitation began. The small colourless plates (7·5 g., 71%) which separated were filtered off, and washed first with a little acetone containing some dimethyl selenide, then with pentane also containing dimethyl selenide. Passage of air through the crystals on a filter plate caused dissociation and appearance of the yellow colour of silver iodide {Found (as above) : Ag, 37·8%. $[Me_2Se(AgI)_2]_n$ requires Ag, 37·3%}. The compound did not melt when heated in a sealed tube, but softened at 84—85° and then gradually became yellow and evolved dimethyl selenide. The compound, which had a strong odour of dimethyl selenide, did not dissolve in any of the usual solvents, and it is probable that both it and the tellurium compound of similar composition have polymeric structures.

Dimethyl telluride forms a compound with cadmium iodide, which was not analysed, but does not combine with anhydrous nickel bromide dissolved in ethanol. Work on dimethyl telluride was abandoned at this stage on account of its rather uncongenial properties.

The author thanks the Director of the Chemical Research Laboratory, Teddington, for the kind loan of the gallium used in this work, and Mr. N. D. Huck of this Department for providing a specimen of pure trimethylaluminium.

THE UNIVERSITY, BRISTOL. [*Received, March 13th*, 1951.]

---

447. *The Chemistry of Fungi. Part XV.* The Degradation of Methyl O-Dimethylcitromycetin.*

By ALEXANDER ROBERTSON, W. B. WHALLEY, and J. YATES.

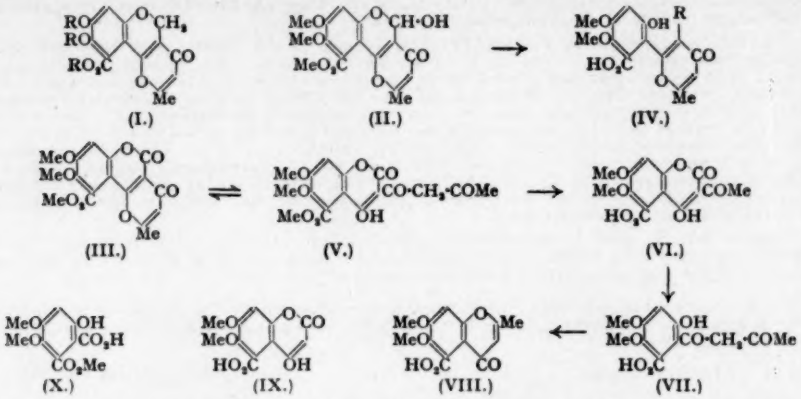
Methyl *O*-dimethylcitromycetin (I; R = Me), which is shown to have basic properties, is oxidised with lead tetra-acetate and chromic acid respectively to give methyl *O*-dimethylcitromycetinol (II) and methyl *O*-dimethylcitromycetinone (III). Unlike *O*-dimethylcitromycin, (I; R = Me) is not oxidised to give (II) and (III) with ozone. The phenylpyrone (IV; R = H) is formed from (II) with alkali, whilst with warm dilute acid (III) gives (V) which on cyclisation regenerates the parent compound. With warm alkali (III) gives rise to (VI), (VIII), and probably (IX), along with acetone and acetic acid.

Attempts to employ the ester (XIV; R = Me, R′ = OH) as the starting material for the synthesis of (VI), (VIII), and (IX) were unsuccessful because (XIV; R = Me, R′ = OH) could not be *C*-formylated or -acetylated. A new route to the synthesis of the acid (XIV; R = H, R′ = OH) is described.

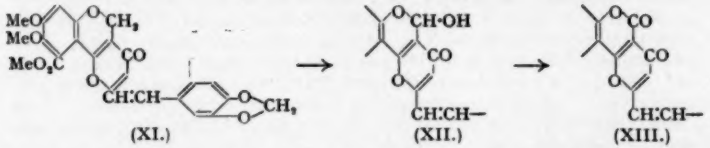
SINCE on oxidation with potassium permanganate methyl *O*-dimethylcitromycetin gave rise to methyl 2-carboxy-3-hydroxy-5 : 6-dimethoxybenzoate (X) (Part III, *J.*, 1949, 848), it became clear that on the basis of the structure established for citromycin (Part XI, *J.*, 1950, 1031; Part XII, *J.*, 1950, 2965) citromycetin was represented by formula (I; R = H). In view of the possibility that the decarboxylation of citromycetin to give citromycin might be accompanied by a fundamental change in the structure of the molecule, it seemed desirable to investigate the stepwise degradation of methyl *O*-dimethylcitromycetin by the methods employed for *O*-dimethylcitromycin with a view to obtaining an analogous series of products. Our efforts have only been partly successful and, though it has been possible to obtain the primary oxidation products (II) and (III) of methyl *O*-dimethylcitromycetin, their decomposition has proved somewhat unsatisfactory (cf. Part XI, *loc. cit.*), a result which is clearly due to the unexpectedly profound effect of the carboxyl (or carbmethoxy-) group present in the benzenoid system. Whilst the structures of the degradation products from (II) and (III) have been deduced primarily from our knowledge of the heterocyclic system in citromycin, the results obtained in the present work serve to support the view that the same heterocyclic system is present in citromycetin.

* Part XIV, *J.*, 1950, 3380.

The basic properties of methyl *O*-dimethylcitromycetin are established by the formation of a picrate, platinichloride, perchlorate, and hydroferric chloride, but the analytical results given by the last two salts are not in agreement with their being the normal derivatives. Like *O*-di-



methylcitromycin (Part VIII, *J.*, 1949, 1567), with lead tetra-acetate methyl *O*-dimethylcitromycetin gave a carbinol base, methyl *O*-dimethylcitromycetinol (II), which readily formed a chloride and on oxidation with chromic acid yielded methyl *O*-dimethylcitromycetinone (III), identical with the product obtained by oxidation of methyl *O*-dimethylcitromycetin with the same reagent; neither of these oxidation products can be obtained by means of ozone (cf. Part III, *loc. cit.*). Methyl *O*-dimethylcitromycetinone retains the basic properties of the parent compound, giving a hydroferric chloride and an abnormal platinichloride, and like *O*-dimethylcitromycinone it forms a dioximino-derivative and an anilide.



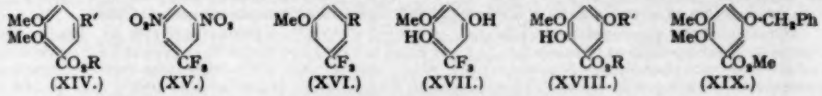
With piperonaldehyde and alcoholic sodium methoxide, methyl *O*-dimethylcitromycetin gives a piperonylidene derivative (XI), which on oxidation with lead tetra-acetate and with chromic acid gives the corresponding derivatives of methyl *O*-dimethylcitromycetinol (XII) and methyl *O*-dimethylcitromycetinone (XIII), respectively, thus showing that the reactive methyl group in the 2-position of the γ-pyrone ring is retained in the oxidation products.

On hydrolysis with warm alkali, methyl *O*-dimethylcitromycetinol (II) gave rise to formic acid and a product which is regarded as the phenyl-γ-pyrone (IV; R = H) formed by the opening of the carbinol ring by way of (IV; R = CHO). On the other hand, the hydrolysis of methyl *O*-dimethylcitromycetinone (III) with warm dilute hydrochloric acid primarily affects the γ-pyrone ring, giving the 3-acetoacetyl-4-hydroxycoumarin (V) which with concentrated sulphuric acid regenerates the parent compound (III) along with a trace of 3-acetyl-4-hydroxy-6 : 7-dimethoxycoumarin-5-carboxylic acid (VI). The hydrolytic decomposition of (III) was also effected with warm alkali under a variety of conditions, and in addition to acetic acid and acetone the main products obtained were the 3-acetyl-4-hydroxycoumarin (VI) and the chromone (VIII), along with small amounts of a substance which may be the 4-hydroxycoumarin (IX) but for which satisfactory analytical results were not obtained.

The structure of the chromone (VIII) is established by the formation of a piperonylidene derivative, confirming the presence of a methyl group in the 2-position, in conjunction with the fission by means of alkali to give two molecular proportions of acetic acid, and the acid (XIV; R = H, R′ = OH). Hydrolytic fission of the compound (VI), which was readily characterised by the formation of the methyl ester, gave the expected products, *viz.*, acetone, acetic acid, the

chromone (VIII), and a trace of the compound believed to be (IX). The chromone (VIII) clearly arises from (VI) and hence from (II) by way of the intermediate diketone (VII) which apparently undergoes cyclisation with remarkable ease.

It seemed desirable that the structures of (VI), (VII), (VIII), and (IX) should be confirmed by synthesis, and for this purpose the acid (XIV; R = H, R′ = OH) appeared to be a suitable starting material. This compound, which was originally obtained by Faltis and Kloiber



(XIV.) (XV.) (XVI.) (XVII.) (XVIII.) (XIX.)

(*Monatsh.*, 1929, **53**, 633) as a by-product during the preparation of 4 : 5-dimethoxybenzene-1 : 2 : 3-tricarboxylic acid from *m*-hemipinic acid, was prepared from (XIV; R = H, R′ = NO_2) by way of (XIV; R = H, R′ = NH_2) and (XIV; R = H, R′ = N_2Cl), but the method gave unsatisfactory results. Although the catalytic reduction of (XIV; R = H, R′ = NO_2) furnished much improved yields of the amine (XIV; R = H, R′ = NH_2), yet the conversion of the corresponding diazonium salt into the phenolic acid (XIV; R = H, R′ = OH) resulted in poor yields accompanied by much by-product. Accordingly, the following superior route was devised. By the action of methanolic sodium hydroxide 3 : 5-dinitrobenzotrifluoride (XV) was converted into 5-methoxy-3-nitrobenzotrifluoride (XVI; R = NO_2), and on catalytic reduction this gave the amine (XVI; R = NH_2) which furnished the 3-hydroxy-5-methoxybenzotrifluoride (XVI; R = OH) by the standard procedure. On oxidation with potassium persulphate this phenol (XVI; R = OH) gave 2 : 5-dihydroxy-3-methoxybenzotrifluoride (XVII), the trifluoromethyl group of which was hydrolysed with alkali (Whalley, *J.*, 1949, 3016) with the formation of the 2 : 5-dihydroxy-3-methoxybenzoic acid (XVIII; R = R′ = H). On monobenzylation, the ester (XVIII; R = Me, R′ = H) of the latter acid furnished the monobenzyl ether which, because of the resistance of phenolic hydroxyl groups in the *o*-position to carboxyl to benzylation, together with the fact that the ether gives a strong ferric reaction, has the orientation (XVIII; R = Me, R′ = Bz). Obtained by the methylation of (XVIII; R = Me, R′ = Bz), methyl 5-benzyloxy-2 : 3-dimethoxybenzoate (XIX) on debenzylation and hydrolysis gave 5-hydroxy-2 : 3-dimethoxybenzoic acid (XIV; R = H, R′ = OH), identical with the compound prepared by the method of Faltis and Kloiber (*loc. cit.*).

Attempts to synthesise (VI), (VIII), and (IX) had to be abandoned when it was found impossible to induce the ester (XIV; R = Me, R′ = OH) to undergo the Gattermann, Hoesch, or Friedel–Crafts reactions. Similarly, the benzotrifluoride (XVII) was equally unreactive.

Experimental.

Derivatives of Methyl O-Dimethylcitromycetin.—(*a*) When a mixture of this ester (1 g.), piperonaldehyde (1 g.), potassium ethoxide (from 0·25 g. of potassium), and alcohol (40 ml.) was heated on the steam-bath for ½ hour and then kept at room temperature for 7 days the *piperonylidene* derivative (0·8 g.) separated. Recrystallised from methanol, this formed bright yellow needles, m. p. 220° (Found: C, 64·8; H, 4·4. $C_{21}H_{20}O_9$ requires C, 64·7; H, 4·3%).

(*b*) Prepared with alcoholic picric acid, the *picrate* of methyl *O*-dimethylcitromycetin separated from methanol or benzene containing a little picric acid in yellow needles, m. p. 164° (Found: C, 49·3; H, 3·5; N, 7·2. $C_{17}H_{16}O_7,C_6H_3O_7N_3$ requires C, 49·2; H, 3·4; N, 7·5%).

(*c*) When a solution of methyl *O*-dimethylcitromycetin (1 g.) and platinum chloride (1 g.) in acetic acid was saturated with hydrogen chloride, the *platinichloride* separated during 2 days in tiny yellow needles, m. p. 191° (decomp.) [Found: C, 38·1; H, 3·5; Cl, 19·4; Pt, 18·1. $(C_{17}H_{16}O_7)_2,H_2PtCl_6$ requires C, 38·0; H, 3·2; Cl, 19·8; Pt, 18·2%].

(*d*) 60% Perchloric acid (1 ml.) was added to a solution of methyl *O*-dimethylcitromycetin (1 g.) in acetic acid (5 ml.), and the resulting *perchlorate*, m. p. 226° (decomp.), was collected 2 days later and washed with a little ether (Found: C, 46·6; H, 4·5; Cl, 20·9. $C_{17}H_{16}O_7,HClO_4$ requires C, 47·2; H, 3·9; Cl, 8·2%).

(*e*) When perchloric acid in (*d*) was replaced by concentrated hydroferrichloric acid, a *salt* separated in dark orange needles, m. p. 161—162° (decomp.), which was collected and washed with a little ether [Found: C, 43·4; H, 4·2; Cl, 19·7; Fe, 8·4. $C_{17}H_{16}O_7,HFeCl_4$ requires C, 38·4; H, 3·2; Cl, 26·7; Fe, 10·5%. $(C_{17}H_{16}O_7)_2,2HFeCl_4$ requires C, 43·9; H, 3·6; Cl, 20·4; Fe, 8·0%]. Attempts to recrystallise this compound or the perchlorate described in (*d*) were unsuccessful.

Methyl O-Dimethylcitromycetinol (II).—A mixture of powdered methyl *O*-dimethylcitromycetin (2 g.) and lead tetra-acetate (4 g.) was kept at 16—18° for 26 days, and the solid isolated from this dark liquor was washed and crystallised from methanol, giving *methyl O-dimethylcitromycetinol* (0·5 g.) in colourless needles, m. p. 234° (decomp.) (Found: C, 58·5; H, 4·8. $C_{17}H_{16}O_8$ requires C, 58·6; H, 4·6%). On addition of water (250 ml.) to the dark acetic acid reaction mixture a further quantity (0·35 g.) of this compound was obtained. Extraction of the aqueous acetic acid liquor with chloroform (100 ml. × 5)

and evaporation of the dried extracts gave a dark brown residue which on crystallisation from warm methanol gave a substance in pale yellow prisms (0·15 g.), m. p. 304—306° (decomp.) (Found : C, 61·3; H, 5·0%). A solution of this product in a little concentrated hydrochloric acid was warmed to 50° for 2 minutes and then diluted with water, giving methyl *O*-dimethylcitromycetinol, m. p. 234° (decomp.) after purification.

This carbinol readily dissolved in a small volume of concentrated hydrochloric acid and on being kept for 12 hours the solution deposited the *chloride* in rosettes of tiny, lemon-yellow prisms, m. p. 242—243° (decomp.) (Found : C, 55·4; H, 4·6; Cl, 9·7. $C_{17}H_{15}O_7Cl$ requires C, 55·6; H, 4·1; Cl, 9·7%). With much water or aqueous sodium acetate the salt regenerated the parent carbinol base.

Oxidation of the piperonylidene derivative of methyl *O*-dimethylcitromycetin (0·9 g.), dissolved in acetic acid (5 ml.), with lead tetra-acetate (2 g.) at room temperature for 28 days gave the *piperonylidene* derivative of methyl *O*-dimethylcitromycetinol, which was isolated with chloroform from the reaction mixture after dilution with water. This compound formed small yellow needles (0·2 g.), m. p. 196—198°, from dilute acetic acid (Found : C, 62·3; H, 4·2. $C_{25}H_{20}O_{10}$ requires C, 62·5; H, 4·2%).

Methyl O-*Dimethylcitromycetinone* (III).—Chromic oxide (0·75 g.) was gradually added to a solution of methyl *O*-dimethylcitromycetin (1 g.) in acetic acid (5 ml.) kept at 70—75°, and next day the green solution was diluted with water (100 ml.), and extracted with chloroform (100 ml. × 5). Evaporation of the combined dried extracts left *methyl* O-*dimethylcitromycetinone* as a brown viscous product which on purification from methanol was obtained in colourless stout prisms (0·6 g.), m. p. 240° (decomp.) [Found : C, 59·3; H, 3·9; OMe, 25·0. $C_{14}H_8O_8(OMe)_3$ requires C, 59·0; H, 4·0; OMe, 26·9%]. Oxidation of methyl *O*-dimethylcitromycetinol (0·4 g.) in acetic acid (2·5 ml.) with chromic oxide (0·3 g.) at 70—75° gave the same product (0·4 g.), m. p. 240° (decomp.), after purification.

Oximation of this compound by the pyridine or sodium acetate method gave a *dioximino*-derivative, which formed colourless flat needles, m. p. 210°, from methanol, having a red ferric reaction (Found : C, 54·4; H, 4·2; N, 7·6. $C_{17}H_{14}O_8N_2$ requires C, 54·3; H, 4·3; N, 7·5%). This compound dissolved in aqueous sodium hydroxide and was recovered unchanged by acidification of the solution. A mixture of methyl *O*-dimethylcitromycetinone (0·5 g.), aniline (1 ml.), and acetic acid (1 ml.) was heated on the steam-bath until a clear solution was formed (about 5 minutes). Treatment of this with an excess of 2N-hydrochloric acid gave an *anilide*, which separated from methanol in tiny, bright yellow needles (0·6 g.), m. p. 226° (Found : C, 63·1; H, 5·2; N, 3·6. $C_{23}H_{21}O_8N$ requires C, 62·9; H, 4·8; N, 3·2%).

Prepared in the usual manner, the *hydroferric chloride* of methyl *O*-dimethylcitromycetinone separated from acetic acid in dark orange prisms, m. p. 152—153° (decomp.) (Found : Cl, 26·1. $C_{17}H_{14}O_8.HFeCl_4$ requires Cl, 26·1%). With platinic chloride in acetic acid methyl *O*-dimethylcitromycetinone gave a complex salt decomposing at 203—204° with darkening at 190° [Found, in specimen dried in a high vacuum at 80° : C, 33·0; H, 3·7; Pt, 10·1. Calc. for $(C_{17}H_{14}O_8)_2.H_2PtCl_6$: C, 37·0; H, 2·7; Pt, 17·7%]. On decomposition with warm aqueous sodium acetate these derivatives gave methyl *O*-dimethylcitromycetinone.

Oxidation of the piperonylidene derivative of methyl *O*-dimethylcitromycetin (0·5 g.), dissolved in acetic acid (2·5 ml.), with chromic oxide (0·4 g.) at 75—80°, followed by the addition of water (100 ml.) gave the *piperonylidene* derivative of methyl *O*-dimethylcitromycetinone. Crystallised from methanol and then dilute acetic acid (charcoal), this compound formed yellow needles (0·3 g.), m. p. 170—172° with darkening [Found : C, 62·6; H, 3·8; OMe, 20·0. $C_{22}H_8O_7(OMe)_3$ requires C, 62·8; H, 3·8; OMe, 19·5%]. Similarly, the oxidation of the piperonylidene derivative of methyl *O*-dimethylcitromycetinol (0·1 g.) with chromic oxide (0·05 g.) in acetic acid (1 ml.) at 70—80° during 3 hours gave the corresponding derivative of methyl *O*-dimethylcitromycetinone, m. p. 170—172° with darkening.

When a solution of methyl *O*-dimethylcitromycetinone (0·5 g.) in methanol (10 ml.) and water (50 ml.) containing Raney nickel (1 g.) was heated under reflux for 2 hours, filtered, evaporated to a small bulk (10 ml.), and kept for 24 hours, a substance separated in pale yellow prisms which, after having been washed with dilute hydrochloric acid to remove a little unchanged material, formed colourless slender needles, m. p. 166°, from methanol, slowly soluble in 2N-aqueous sodium hydrogen carbonate and readily soluble in dilute sodium hydroxide (Found : C, 58·3, 58·3; H, 5·4, 5·3; OMe, 27·8%). When a solution of this compound in concentrated sulphuric acid was kept at room temperature for 2 hours and then poured on ice, methyl *O*-dimethylcitromycetinone, m. p. 240° (decomp.), was regenerated. On being heated with aniline, the substance, m. p. 166°, gave rise to the anilide, m. p. 226°, identical with that obtained from methyl *O*-dimethylcitromycetinone.

Degradation of Methyl O-*Dimethylcitromycetinol with Alkali.* (With G. W. K. Cavill.)—This compound (1·3 g.) was heated under reflux with 2N-aqueous sodium hydroxide (50 ml.) in an atmosphere of nitrogen for 1½ hours; the solid had dissolved in about 15 minutes, giving a clear amber solution. Acidification of the cooled reaction mixture with 2N-sulphuric acid (100 ml.) yielded a flocculent buff-coloured precipitate (0·6 g.) which was extracted with warm methanol, leaving 2-(6-*carboxy*-2-*hydroxy*-4 : 5-*dimethoxyphenyl*)-6-*methyl*-4-*pyrone* (0·1 g.). Crystallised from dioxan, this compound formed colourless prisms, m. p. 225—228° (decomp.) (Found : C, 58·6; H, 4·8. $C_{13}H_{14}O_7$ requires C, 58·8; H, 4·6%). This pyrone, which forms a yellow solution in a little concentrated hydrochloric acid, is soluble in 2N-aqueous sodium hydrogen carbonate and gives an incipient ferric reaction in alcohol.

From the methanolic extract of the precipitate 5-*carboxy*-6 : 7-*dimethoxy*-2-*methylchromone* (0·3 g.) separated in very pale yellow needles (0·3 g.), m. p. 156°, after recrystallisation (Found : C, 59·1; H, 4·6. $C_{13}H_{12}O_6$ requires C, 59·1; H, 4·6%). Treatment of the filtered acidic liquor left after the isolation of the precipitate with aqueous 2 : 4-dinitrophenylhydrazine sulphate gave a yellow precipitate from which acetone 2 : 4-dinitrophenylhydrazone (0·15 g.) was isolated by chromatography from light petroleum on aluminium oxide and identified by comparison with an authentic specimen. Distillation of the aqueous filtrate from the crude hydrazone gave formic acid, which was identified by conversion into the benziminazole (0·2 g.), m. p. 168—170°, after purification (Found : N, 23·3. Calc. for $C_7H_6N_2$:

N, 23·7%). A portion of the benziminazole was converted into the picrate, m. p. 223—225° (decomp.), identical with an authentic specimen.

Hydrolysis of Methyl O-Dimethylcitromycetinone.—(*a*) A solution of this compound (1 g.) in concentrated hydrochloric acid (50 ml.) was heated on the steam-bath for 1½ hours, cooled, diluted with water (100 ml.), almost neutralised with 2N-aqueous sodium hydroxide (150 ml.), and quickly extracted with ether (50 ml. × 20). The residue left on the evaporation of the combined dried extracts was washed several times with cold dilute hydrochloric acid to remove traces of methyl *O*-dimethylcitromycetinone and then crystallised from ethyl acetate–light petroleum, giving *methyl 3-acetoacetyl-4-hydroxy-6 : 7-dimethoxycoumarin-5-carboxylate* (V) in colourless needles, m. p. 165·5° (decomp.) (Found : C, 55·8; H, 4·6. $C_{17}H_{16}O_9$ requires C, 56·0; H, 4·4%); the yield of this product varied from about 50 to 100 mg. This diketone, which had a pale yellow-orange ferric reaction in alcohol, dissolved readily in 2N-aqueous sodium carbonate or hydroxide and slowly in aqueous 2N-sodium hydrogen carbonate. Treatment of the compound (50 mg.) with concentrated sulphuric acid (5 ml.) at room temperature for 24 hours followed by the addition of ice regenerated methyl *O*-dimethylcitromycetinone (40 mg.), m. p. and mixed m. p. 240° (decomp.), after purification (Found : C, 59·0; H, 4·3%).

(*b*) Methyl *O*-dimethylcitromycetinone (1 g.) was warmed with 2N-aqueous sodium hydroxide (50 ml.) on the steam-bath for 10 minutes and the resulting deep orange solution was cooled and acidified with 2N-sulphuric acid. After having been washed and dried, the yellow precipitate (0·6 g.) was extracted with hot methanol, giving 6 : 7-*dimethoxy-2-methylchromone-5-carboxylic acid* in pale yellow needles (0·36 g.), m. p. 156°, readily soluble in aqueous sodium hydrogen carbonate or ether, and moderately soluble in water or warm methanol [Found : C, 59·0; H, 5·0; OMe, 24·8. $C_{11}H_8O_4(OMe)_2$ requires C, 59·1; H, 4·6; OMe, 23·5%]. Interaction of a solution of the sodium salt of this acid (from 0·2 g. of acid) in 50% methanol (10 ml.) with *p*-nitrobenzyl bromide (0·3 g.) on the steam-bath for 1½ hours gave rise to the p-*nitrobenzyl* ester, which formed almost colourless needles, m. p. 168°, from alcohol (Found : C, 60·5; H, 4·1. $C_{20}H_{17}O_8N$ requires C, 60·1; H, 4·3%). Condensation of 6 : 7-dimethoxy-2-methylchromone-5-carboxylic acid (0·5 g.) and piperonaldehyde (0·5 g.) with methanolic sodium methoxide (from 0·25 g. of sodium and 50 ml. of methanol) on the steam-bath during 1 hour furnished a *piperonylidene* derivative which separated from benzene in clusters of pale yellow needles (0·15 g.), m. p. 225·5°, slowly soluble in aqueous sodium hydrogen carbonate (Found, in specimen dried in a high vacuum at 80° : C, 61·1; H, 3·9. $C_{21}H_{16}O_8$ requires C, 60·9; H, 4·4%).

The residue left after the extraction of 6 : 7-dimethoxy-2-methylchromone-5-carboxylic acid was crystallised from a large volume of methanol, giving *3-acetyl-4-hydroxy-6 : 7-dimethoxycoumarin-5-carboxylic acid* in colourless needles (0·2 g.), m. p. 314° (decomp.), soluble in aqueous sodium hydrogen carbonate and giving a brownish ferric reaction in alcohol [Found : C, 54·8; H, 4·9; OMe, 18·5. $C_{13}H_8O_6(OMe)_2$ requires C, 54·6; H, 3·9; OMe, 19·8%]. This compound did not react with 2 : 4-dinitrophenylhydrazine but on methylation with ethereal diazomethane or methyl iodide–potassium carbonate gave *methyl 3-acetyl-4-hydroxy-6 : 7-dimethoxycoumarin-5-carboxylate*, which formed colourless prisms, m. p. 229° (decomp.), from methanol [Found : C, 55·9; H, 4·5; OMe, 26·6. $C_{13}H_8O_6(OMe)_2$ requires C, 55·9; H, 4·4; OMe, 28·3%].

The acidic liquor remaining after the separation of the solid precipitate was diluted with water and repeatedly extracted with ether, giving more 6 : 7-dimethoxy-2-methylchromone-5-carboxylic acid (0·32 g.). From the aqueous liquor, acetone, as its 2 : 4-dinitrophenylhydrazone, and acetic acid, as 2-methylbenziminazole (Brown and Campbell, *J.*, 1937, 1699), were isolated.

(*c*) Methyl *O*-dimethylcitromycetinone (8 g.) was heated under reflux with 2N-sodium hydroxide (400 ml.) for 1½ hours, and the cooled solution acidified with 2N-sulphuric acid (500 ml.), giving a precipitate of 6 : 7-dimethoxy-2-methylchromone-5-carboxylic acid (2·3 g.), m. p. 156°, after purification from methanol. From portions of the aqueous filtrate the acetone and acetic acid were isolated, whilst extraction with ether yielded more 6 : 7-dimethoxy-2-methylchromone-5-carboxylic acid along with a small amount of a white solid (0·05 g.) which on repeated crystallisation from methanol gave a compound in rhombic prisms, m. p. 255°, which may be impure 4-hydroxy-6 : 7-dimethoxycoumarin-5-carboxylic acid (Found : C, 55·5; H, 5·1; OMe, 15·8%).

Degradation of 3-Acetyl-4-hydroxy-6 : 7-dimethoxycoumarin-5-carboxylic Acid.—The coumarin (1 g.) was refluxed with 10% aqueous sodium hydroxide (50 ml.) in a stream of nitrogen which was led into aqueous-alcoholic 2 : 4-dinitrophenylhydrazine sulphate for 1½ hours. The latter solution gave a precipitate of acetone 2 : 4-dinitrophenylhydrazone, m. p. 128°, after purification. The cooled alkaline hydrolysate was acidified with 2N-sulphuric acid, giving a precipitate of 6 : 7-dimethoxy-2-methylchromone-5-carboxylic acid (0·05 g.), m. p. 156°, after sublimation in a high vacuum. Extraction of the acidic liquor with ether gave a product containing more of this chromone along with a small amount of the compound, m. p. 255°, believed to be 4-hydroxy-6 : 7-dimethoxycoumarin-5-carboxylic acid. In another experiment acetic acid was isolated and converted into 2-methylbenziminazole, m. p. 170—173°, and the picrate, m. p. 212—213° (decomp.).

Degradation of 6 : 7-Dimethoxy-2-methylchromone-5-carboxylic Acid.—A mixture of the chromone (1·8 g.) and 50% aqueous potassium hydroxide (20 ml.) was kept at 120—130° for ½ hour and then at 310—320° for 30 minutes in a stream of nitrogen which was led through aqueous-alcoholic 2 : 4-dinitrophenylhydrazine sulphate. From the latter, only a trace of a 2 : 4-dinitrophenylhydrazone was obtained. The alkaline melt was dissolved in water (100 ml.) and acidified with 2N-sulphuric acid. From a portion of the aqueous liquor, acetic acid equivalent to two molecular proportions was isolated and converted into methylbenziminazole, m. p. 170—173°, and thence into its picrate, m. p. 213° (decomp.). From the remainder of the filtrate 2 : 3-dimethoxy-5-hydroxybenzoic acid, m. p. 175—178°, after purification, was isolated and identified by comparison with an authentic specimen.

3-Amino-5-methoxybenzotrifluoride.—A mixture of 3 : 5-dinitrobenzotrifluoride (Finger and Reed, *J. Amer. Chem. Soc.*, 1944, **66**, 1972) (10 g.), sodium methoxide (5·4 g.), and methanol (50 ml.) was heated

under reflux for 1 hour, most of the solvent was distilled, and after the addition of water (120 ml.) the mixture was extracted with ether, giving an orange-red product. Distillation of this in a high vacuum gave *3-methoxy-5-nitrobenzotrifluoride*, which formed colourless rectangular prisms (8·5 g.), m. p. 37·5°, from light petroleum (b. p. 60—80°) (Found: C, 42·8; H, 3·5; N, 6·5; F, 25·9. $C_8H_6O_3NF_3$ requires C, 43·4; H, 2·7; N, 6·3; F, 25·8%). This product was identical with that prepared by methylation of 3-hydroxy-5-nitrobenzotrifluoride (Whalley, *loc. cit.*).

Reduction of this compound (5 g.), dissolved in methanol (100 ml.), with hydrogen and palladium–charcoal catalyst (from 1 g. of charcoal and 0·1 g. of palladium chloride) gave *3-amino-5-methoxybenzotrifluoride*, which formed long, colourless, silky needles, m. p. 151°, from light petroleum (b. p. 60—80°), soluble in dilute hydrochloric acid, water, and organic solvents (Found: N, 7·3. $C_8H_8ONF_3$ requires N, 7·3%). Prepared with acetic anhydride, the *acetyl* derivative separated from benzene in long, colourless needles, m. p. 120° (Found: C, 51·5; H, 4·2; N, 6·2; F, 24·8. $C_{10}H_{10}O_2NF_3$ requires C, 51·5; H, 4·3; N, 6·0; F, 24·5%).

3-Hydroxy-5-methoxybenzotrifluoride.—3-Amino-5-methoxybenzotrifluoride (5 g.) was dissolved in 2N-hydrochloric acid (100 ml.) at 0° and converted into the diazonium chloride with a solution of sodium nitrite (1·95 g.) in water (10 ml.). After 15 minutes the excess of nitrous acid was destroyed with urea, and the solution mixed with sulphuric acid (from 200 ml. of concentrated acid and 200 ml. of water) and heated to 95° for 1½ hours. On isolation with ether the resulting *3-hydroxy-5-methoxybenzotrifluoride* was purified by distillation, crystallisation from light petroleum, and finally by sublimation at 100°/14 mm., forming rectangular prisms (3·4 g.), m. p. 75° (Found: C, 49·7; H, 4·2; F, 30·4. $C_8H_7O_2F_3$ requires C, 50·0; H, 3·7; F, 29·7%). The p-*nitrobenzoate* formed clusters of slender, pale yellow needles, m. p. 115° (Found: N, 4·2. $C_{15}H_{10}O_5NF_3$ requires N, 4·1%).

2 : 5-Dihydroxy-3-methoxybenzotrifluoride.—Saturated aqueous solution containing potassium persulphate (14·1 g.) was added to a stirred solution of 3-hydroxy-5-methoxybenzotrifluoride (10 g.) in 10% aqueous sodium hydroxide at 18° in the course of 3—4 hours. After 24 hours the mixture was acidified (Congo-red) with hydrochloric acid, extracted with ether to remove unchanged phenol (5 g.), and after the addition of concentrated hydrochloric acid was again extracted with ether, giving *2 : 5-dihydroxy-3-methoxybenzotrifluoride* (4 g.) which was sublimed at 140°/0·2 mm. Crystallised from benzene, this quinol formed colourless flat prisms, m. p. 131°, giving a red-brown ferric reaction (Found: C, 46·2; H, 3·4; F, 27·5. $C_8H_7O_3F_3$ requires C, 46·2; H, 3·4; F, 27·4%). The *di*-p-*nitrobenzoate* separated from dilute methanol in almost colourless prisms, m. p. 194° (Found: N, 5·6. $C_{22}H_{13}O_9N_2F_3$ requires N, 5·5%).

2 : 5-Dihydroxy-3-methoxybenzoic Acid.—A solution of 2 : 5-dihydroxy-3-methoxybenzotrifluoride (7·7 g.) in 2N-aqueous sodium hydroxide (100 ml.) was kept for 24 hours, acidified, and extracted with ether. From the combined ethereal extracts *2 : 5-dihydroxy-3-methoxybenzoic acid* (5·6 g.) was isolated by means of aqueous sodium hydrogen carbonate and purified by sublimation at 210°/0·2 mm. and then by crystallisation from light petroleum, forming colourless needles, m. p. 221°, with an olive-green ferric reaction in alcohol (Found: C, 52·0; H, 4·6. $C_8H_8O_5$ requires C, 52·2; H, 4·3%). Formed with ethereal diazomethane, the *methyl* ester separated from benzene–light petroleum in colourless prisms, m. p. 163·5°, having a dark green ferric reaction in alcohol [Found: C, 54·7; H, 5·1; OMe, 30·0. $C_7H_4O_3(OMe)_2$ requires C, 54·5; H, 5·1; OMe, 31·3%]. The *di*-p-*nitrobenzoate* crystallised from methanol in fawn-coloured prisms, m. p. 209° (Found: C, 55·8; H, 3·5; N, 5·5. $C_{22}H_{14}O_{11}N_2$ requires C, 55·6; H, 3·2; N, 5·6%).

Methyl 5-Hydroxy-2 : 3-dimethoxybenzoate.—Benzylation of methyl 2 : 5-dihydroxy-3-methoxybenzoate (25 g.) with benzyl bromide (18 ml.) and potassium carbonate (25 g.) in boiling acetone (1·5 l.) was accomplished during 5 hours. On isolation, the *methyl 5-benzyloxy-2-hydroxy-3-methoxybenzoate* was purified by chromatography from ether (1 l.) on aluminium oxide, followed by distillation at 180—182°/0·1 mm., and then by crystallisation from light petroleum, and obtained in colourless needles (18 g.), m. p. 102°, having a dark green ferric reaction (Found: C, 66·4; H, 5·5. $C_{16}H_{16}O_5$ requires C, 66·7; H, 5·6%). The p-*nitrobenzoate* separated from benzene–light petroleum (b. p. 60—80°) in colourless plates, m. p. 182° (Found: N, 3·6. $C_{23}H_{19}O_8N$ requires N, 3·2%).

Methylation of this benzyl ether (18 g.) with potassium carbonate (20 g.) and an excess of methyl iodide in boiling acetone (1 l.) during 20 hours and distillation of the product gave *methyl 5-benzyloxy-2 : 3-dimethoxybenzoate* as a pale yellow oil (18 g.), b. p. 195—196°/0·3 mm. [Found: C, 67·0; H, 5·3; OMe, 28·4. $C_{16}H_8O_2(OMe)_3$ requires C, 67·6; H, 6·0; OMe, 30·8%]. Debenzylation of this compound (5 g.), dissolved in acetic acid (100 ml.), with hydrogen and a palladium–charcoal catalyst (from 0·2 g. of palladium chloride and 2 g. of charcoal) was complete in 2 hours and gave *methyl 5-hydroxy-2 : 3-dimethoxybenzoate* as a pale yellow oil (3·4 g.), b. p. 145°/0·4 mm. (Found: C, 56·8; H, 5·6. $C_{10}H_{12}O_5$ requires C, 56·6; H, 5·7%). This product was readily soluble in dilute aqueous sodium hydroxide and gave a transient pale green ferric reaction. The p-*nitrobenzoate* formed pale yellow prisms, m. p. 126°, from benzene–light petroleum (Found: N, 3·9. $C_{17}H_{15}O_8N$ requires N, 3·9%). When the debenzylation was carried out with half the amount of catalyst during 7 hours the product was unexpectedly 5-hydroxy-2 : 3-dimethoxybenzoic acid, pale yellow irregular prisms, m. p. 178° (Found: C, 54·7; H, 5·1. Calc. for $C_9H_{10}O_5$: C, 54·5; H, 5·1%). A specimen prepared according to Faltis and Kloiber (*loc. cit.*), who give m. p. 186—188°, had m. p. 178°, and was identical with the foregoing acid.

Debenzylation of methyl 5-benzyloxy-2 : 3-dimethoxybenzoate (1 g.) with acetic acid (2 ml.) and concentrated hydrochloric acid (2 ml.) during 10 minutes gave rise to a mixture of unchanged compound and 5-hydroxy-2 : 3-dimethoxybenzoic acid, m. p. 178°.

We are indebted to Imperial Chemical Industries Limited, Widnes, for a gift of benzotrifluoride and to the Department of Scientific and Industrial Research for a maintenance grant to one of us (J. Y.).

UNIVERSITY OF LIVERPOOL. [*Received, March 28th,* 1951.]

448. *Some Alkylresorcinols.*

By J. P. Brown, D. H. Johnson, Alexander Robertson, and W. B. Whalley.

A number of alkylresorcinols, mainly of formula $C_9H_{12}O_2$, have been prepared in the course of the identification of 5-ethyl-4-methylresorcinol from citrinin (*loc. cit.*). The phenols have been characterised by the formation of di-*p*-nitrobenzoates.

The isomeric alkylresorcinols $C_9H_{12}O_2$ and their derivatives described in the present communication were synthesised in the course of studies on the identification of 5-ethyl-4-methylresorcinol obtained originally by the degradation of citrinin (*J.*, 1949, 859). Except in the case of 5-ethyl-2-methylresorcinol, the phenols described have been characterised by the formation of di-*p*-nitrobenzoates as well as by the formation of bisphenylazo-derivatives in some instances. In connection with the three isomeric *iso*propylresorcinols it is of interest that Meyer and Bernhauer (*Monatsh.*, 1929, **53**, 721) obtained an *iso*propylresorcinol, m. p. 107°, believed to be probably 4-*iso*propylresorcinol by the condensation of resorcinol and *iso*propyl alcohol with sulphuric acid. Repetition of this experiment gave a compound, m. p. 107—108°, which was not identical with either 2-*n*-propyl-, 4-*iso*propyl-, or 5-*iso*propyl-resorcinol.

Experimental.

4-Ethyl-2-methylresorcinol.—3-Ethyl-6-methoxy-*o*-cresol (Me = 1) (3·6 g.) was prepared from 2-hydroxy-4-methoxy-3-methylacetophenone (Rangaswami and Seshadri, *Proc. Indian Acad. Sci.*, 1938, **8**, *A*, 214) by the method of Robinson and Shah (*J.*, 1934, 1491) and on demethylation with boiling hydriodic acid (25 ml.; *d* 1·7) and acetic acid (from 15 ml. of acetic anhydride) for ½ hour gave rise to 4-ethyl-2-methylresorcinol which was purified by distillation in a vacuum (b. p. 108°/0·4 mm.) and then by crystallisation from benzene–light petroleum (b. p. 60—80°), forming needles, m. p. 92—93° (Found: C, 71·0; H, 8·2. Calc. for $C_9H_{12}O_2$: C, 71·0; H, 8·0%) (cf. Robinson and Shah, *loc. cit.*, who give m. p. 88—90°). This compound was also prepared by Clemmensen reduction of 2 : 4-dihydroxy-3-methylacetophenone. The *di*-p-*nitrobenzoate* separated from alcohol in pale yellow needles, m. p. 146° (Found: N, 6·6. $C_{23}H_{16}O_8N_2$ requires N, 6·2%).

5-Ethyl-2-methylresorcinol.—A well stirred mixture of 3 : 5-dimethoxy-4-methylacetophenone (0·8 g.) (*J.*, 1950, 2971), benzene (25 ml.), concentrated hydrochloric acid (25 ml.), and amalgamated zinc (7 g.) was heated on the steam-bath for 2½ hours. Dimethyl ether of 5-ethyl-2-methylresorcinol was obtained as a pale orange oil (0·6 g.) which on demethylation with boiling hydriodic acid (10 ml.; *d* 1·7) and acetic acid (from 6 ml. of anhydride) gave *5-ethyl-2-methylresorcinol* which was obtained in prismatic needles, m. p. 121—122°, after repeated sublimation at 120—130°/0·05 mm., having a transient blue ferric reaction in aqueous alcohol (Found: C, 71·3; H, 8·2. $C_9H_{12}O_2$ requires C, 71·0; H, 8·0%).

2-Ethyl-4-methylresorcinol.—3-Ethyl-2 : 4-dihydroxybenzaldehyde (cf. Robinson and Shah, *loc. cit.*) had m. p. 122° and on reduction gave 2-ethyl-4-methylresorcinol, m. p. 99—100°, which gave a *di*-p-*nitrobenzoate*, prisms, m. p. 158—159° (from alcohol) (Found: N, 6·3%).

2-Ethyl-5-methylresorcinol.—This phenol (Desai and Vakil, *Proc. Indian Acad. Sci.*, 1940, **12**, *A*, 39, who give m. p. 135°) formed rosettes of needles, m. p. 132°, from benzene and had a blue ferric reaction in water. The *di*-p-*nitrobenzoate* separated from alcohol–ethyl acetate in prisms, m. p. 163—164° (Found: N, 6·3%), and the *bisphenylazo*-derivative in orange leaflets, m. p. 192°, from light petroleum (Found: N, 15·4. $C_{21}H_{20}O_2N_4$ requires N, 15·6%).

4-Ethyl-5-methylresorcinol.—Prepared by the method of Robinson and Shah (*loc. cit.*) who give m. p. 75—80°, 4-ethyl-5-methylresorcinol formed needles, m. p. 82—83°, from benzene and gave a *di*-p-*nitrobenzoate*, separating from alcohol in needles, m. p. 171—171·5° (Found: C, 61·5; H, 4·2; N, 5·9. $C_{23}H_{18}O_8N_2$ requires C, 61·3; H, 4·0; N, 6·2%). On being warmed with diazoaminobenzene (1·2 g.) in alcohol (15 ml.) on the steam-bath for 1 hour this phenol (0·2 g.) gave rise to the *bisphenylazo*-derivative which formed red needles, m. p. 184°, from alcohol and orange plates, m. p. 193°, from light petroleum (Found: C, 69·7; H, 5·8; N, 15·7. $C_{21}H_{20}O_2N_4$ requires C, 70·0; H, 5·6; N, 15·6%).

4-Ethyl-6-methylresorcinol.—This compound was prepared by the reduction of 2 : 4-dihydroxy-5-ethylbenzaldehyde, m. p. 134°, and obtained as a colourless oil, b. p. 110°/0·05 mm., which crystallised in needles, m. p. 56° (Found: C, 70·9; H, 8·2%) (cf. Robinson and Shah, *loc. cit.*, who give m. p. 60—63°). Purification of this phenol from benzene–light petroleum gave material containing solvent of crystallisation. The *di*-p-*nitrobenzoate* separated from dilute alcohol or acetic acid in pale yellow, slender needles, m. p. 148—149° (Found: C, 61·2; H, 4·0; N, 6·1%).

The *di*-p-*nitrobenzoate* of 2-*n*-propylresorcinol (Limaye and Shenoliker, *Rasayanam*, 1936, **1**, 93) separated from alcohol in pale yellow prisms, m. p. 163° (Found: N, 6·1. $C_{23}H_{18}O_8N_2$ requires N, 6·2%).

Contrary to Sonn (*Ber.*, 1921, **54**, 774), who stated that 4-*n*-propylresorcinol had m. p. 107—108°, whilst the solvated compound had m. p. 71°, we found that, prepared by the method of Johnson and Lane (*J. Amer. Chem. Soc.*, 1921, **43**, 357), who give m. p. 78°, this phenol had m. p. 78—79°. The *di*-p-*nitrobenzoate* formed rosettes of pale yellow needles, m. p. 133°, from alcohol (Found: N, 6·4%). The *bisphenylazo*-derivative separated from light petroleum in crimson needles, m. p. 168° (Found: N, 15·7. $C_{21}H_{20}O_2N_4$ requires N, 15·6%).

5-*Ethyl*-4-n-*propylresorcinol*.—The interaction of 5-ethylresorcinol (2 g.), propionitrile (1·5 g.), and zinc chloride (2·5 g.) in ether (100 ml.), saturated with hydrogen chloride, during 2 days gave an oil which was washed with ether by decantation. A solution of this product in water (75 ml.) was almost neutralised with sodium hydrogen carbonate and then heated on the steam-bath for 45 minutes, giving 5-*ethyl*-2 : 4-*dihydroxy*-n-*propiophenone* which formed colourless prisms (0·6 g.), m. p. 142°, from benzene and had a red-brown ferric reaction in alcohol (Found: C, 68·2; H, 7·5. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·2%). Reduction of this ketone (0·5 g.), by Clemmensen's method gave 5-*ethyl*-4-n-*propylresorcinol*, separating from benzene–light petroleum in glistening plates, m. p. 78° (Found: C, 73·5; H, 9·1. $C_{11}H_{16}O_2$ requires C, 73·3; H, 8·9%). The *di*-p-*nitrobenzoate* crystallised from alcohol in long colourless needles, m. p. 148° (Found: C, 62·6; H, 4·8; N, 6·1. $C_{25}H_{22}O_8N_2$ requires C, 62·8; H, 4·7; N, 5·9%), and the *bisphenylazo*-derivative in scarlet needles, m. p. 181° (Found: N, 14·5. $C_{23}H_{24}O_2N_4$ requires N, 14·4%).

2-iso*Propylresorcinol*.—A solution of 2 : 6-dimethoxyacetophenone (Sugusawa, *J.*, 1934, 1483) (6·2 g.) in benzene (90 ml.) was added to well-stirred ethereal methylmagnesium iodide (from 5 g. of magnesium, 35 g. of methyl iodide, and 100 ml. of ether), the ether was evaporated, the benzene liquor was heated under reflux on the steam-bath for 4 hours, and then after the evaporation of the benzene the viscous residue was kept at 100° for 2 hours. Next day the product was covered with ether (100 ml.) and decomposed with saturated aqueous ammonium chloride (100 ml.). On isolation with ether the resulting 2-(2 : 6-*dimethoxyphenyl*)*propene* was obtained as a colourless oil (5·9 g.), b. p. 106—110°/0·15 mm. (Found: C, 74·3; H, 8·1. $C_{11}H_{14}O_2$ requires C, 74·1; H, 7·9%). Hydrogenation of this propene (5 g.), dissolved in methanol (150 ml.), with the palladium–charcoal catalyst gave rise to 2-(2 : 6-*dimethoxyphenyl*)*propane* as a colourless oil (4·7 g.), b. p. 71—73°/0·05 mm. (Found: C, 73·2; H, 9·1. $C_{11}H_{16}O_2$ requires C, 73·3; H, 8·9%).

Demethylation of the foregoing propane derivative (1·6 g.) with boiling hydriodic acid (25 ml., *d* 1·7) and acetic acid (from 15 ml. of anhydride) during ½ hour furnished 2-iso*propylresorcinol*, b. p. 114°/0·05 mm., which crystallised from benzene–light petroleum in rosettes of colourless needles, m. p. 82°, having a pale blue ferric reaction in water (Found: C, 71·2; H, 8·2. $C_9H_{12}O_2$ requires C, 71·0; H, 8·0%). The *di*-p-*nitrobenzoate* separated from acetic acid in pale yellow small needles, m. p. 184—185° (Found: N, 6·2%).

4-iso*Propylresorcinol*.—Prepared from 2 : 4-dimethoxyacetophenone (4 g.) by the method employed for 2-(2 : 6-dimethoxyphenyl)propene, 2-(2 : 4-*dimethoxyphenyl*)*propene* (3 g.) was obtained as a colourless pungent oil, b. p. 170°/10 mm. (Found: C, 73·6; H, 8·2%), which on hydrogenation, yielded 2-(2 : 4-dimethoxyphenyl)propane. Demethylation of the foregoing propane (2 g.) in the usual manner furnished 4-iso*propylresorcinol* which was purified by distillation in a vacuum and then by crystallisation from benzene, forming large colourless prisms (1·1 g.), b. p. 114°/0·2 mm., m. p. 98°, moderately soluble in benzene or water and giving a blue ferric reaction in water (Found: C, 70·9; H, 8·1%). The *di*-p-*nitrobenzoate* separated from acetic acid in needles, m. p. 124° (Found: C, 61·3; H, 4·0; N, 6·2%), and the *bisphenylazo*-derivative from alcohol in two interconvertible forms: (*a*) flocculent orange needles, m. p. 186° with sintering at 166°, and (*b*) purple-red needles, m. p. 186° after sintering at 183° (Found: C, 70·0; H, 5·7; N, 15·6. $C_{21}H_{20}O_2N_4$ requires C, 70·0; H, 5·6; N, 15·6%).

5-iso*Propylresorcinol*.—The quantitative formation of methyl 3 : 5-dimethoxybenzoate from the parent acid with diazomethane was found to be superior to Seka and Fuchs's lengthy esterification process (*Monatsh.*, 1931, **57**, 65). This ester (10·1 g.) was heated under reflux with ethereal methylmagnesium iodide (from 14·7 g. of magnesium, 43 ml. of methyl iodide, and 360 ml. of ether) for 6 hours and the mixture treated with ice and aqueous ammonium chloride. The resulting 2-(3 : 5-*dimethoxyphenyl*)-*propene* was purified by distillation and obtained as a colourless oil (5·9 g.), b. p. 134°/15 mm. (Found: C, 74·4; H, 8·1. $C_{11}H_{14}O_2$ requires C, 74·0; H, 7·9%). On hydrogenation with a palladium–charcoal catalyst this compound gave a quantitative yield of 2-(3 : 5-*dimethoxyphenyl*)*propane*, a colourless oil, b. p. 125°/1·4 mm. (Found: C, 73·6; H, 9·2. $C_{11}H_{16}O_2$ requires C, 73·3; H, 8·9%).

Demethylation of the foregoing propane derivative (4 g.) by boiling concentrated hydriodic acid–acetic acid during ½ hour furnished 5-iso*propylresorcinol* which was purified by distillation and then by crystallisation from benzene, forming colourless prisms (2·7 g.), b. p. 120°/0·15 mm., m. p. 110°, readily soluble in water and having a violet ferric reaction in alcohol (Found: C, 71·3; H, 8·1%). The *di*-p-*nitrobenzoate* separated from acetic acid in pale cream-coloured prisms, m. p. 183° (Found: C, 61·2; H, 4·2; N, 6·1%), and the *bisphenylazo*-derivative from alcohol in orange needles, m. p. 190° (Found: C, 70·0; H, 5·2; N, 15·3%).

Colour Reactions of Alkylresorcinols.—In examining qualitative methods for the differentiation of substituted resorcinols it has been observed that with aqueous bleaching powder resorcinol, orcinol, 5-ethyl-, 5-*n*-propyl-, and 5-*iso*propyl-resorcinol give cherry-red colours fading to reddish-brown, whereas γ-alkylresorcinols, *e.g.*, 2-methyl-, 2-ethyl-, 2-*n*-propyl-, 2-*iso*propyl-, 2-ethyl-4-methyl-, 2-ethyl-5-methyl-, and 4-ethyl-2-methyl-resorcinol, give comparatively stable red or bluish-red colours. On the other hand, yellow or orange-yellow colours are given by β-substituted resorcinols of the following types: 4-methyl-, 4-*n*-propyl-, 5-ethyl-4-methyl-, 6-ethyl-4-methyl-, and 4-ethyl-5-methyl-resorcinol.

We are indebted to the Department of Scientific and Industrial Research for a maintenance grant to one of us (D. H. J.).

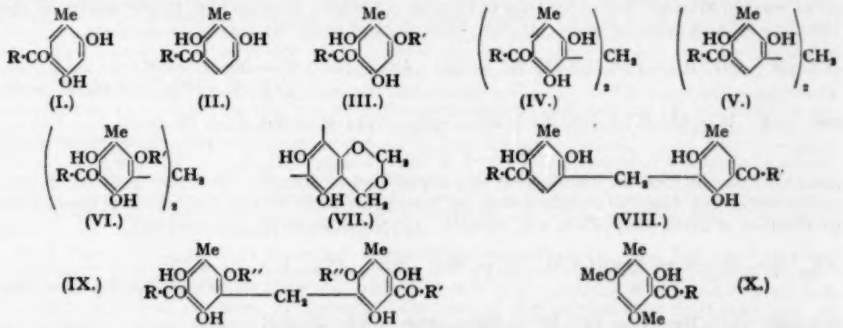
UNIVERSITY OF LIVERPOOL. [*Received, March 28th*, 1951.]

449. *Rottlerin. Part VIII.* The Rottlerone Change.*

By Alexander McGookin, Alexander Robertson, and T. H. Simpson.

In earlier papers (for references see text) it was shown that rottlerin and its hydrogenation products were unsymmetrical polyhydroxydiarylmethanes which underwent the reversible rottlerone change. In order to investigate the general applicability of this reaction a series of symmetrical and unsymmetrical polyhydroxydiphenylmethanes, types (V), (VI), and (VIII), have been synthesised by the standard procedure. The majority of these compounds have been shown to disproportionate in the expected manner. In general, the diphenylmethanes derived from phloroglucinol react more readily than those from resorcinol. Further, the unsymmetrical polyhydroxydiphenylmethanes which can be formed by reversing the rottlerone change are those which can be synthesised from two dissimilar ketones by the phenol–formaldehyde reaction. The decomposition of polyhydroxydiphenylmethanes according to the scheme $R{\cdot}CH_2{\cdot}R + 2R'H \longrightarrow R'{\cdot}CH_2{\cdot}R' + 2RH$ has also been studied.

In earlier papers in this series (Part II, *J.*, 1938, 309; Part IV, *J.*, 1939, 1579; Part V, *J.*, 1939, 1587) it has been shown that rottlerin and its hydrogenation products are unsymmetrical polyhydroxydiarylmethanes of the type $R{\cdot}CH_2{\cdot}R'$ which, on treatment with warm acidic or alkaline reagents, undergo disproportionation according to the scheme $2R{\cdot}CH_2{\cdot}R' \longrightarrow R{\cdot}CH_2{\cdot}R + R'{\cdot}CH_2{\cdot}R'$, *i.e.*, the rottlerone change. In the case of the hydrogenation products this reaction is best effected by boiling acetic acid, with which the formation of resinous by-products is much less marked. Further, with the aid of this reagent it was possible to establish the reversibility of the reaction, thus: $2R{\cdot}CH_2{\cdot}R' \rightleftharpoons R{\cdot}CH_2{\cdot}R + R'{\cdot}CH_2{\cdot}R'$ (Part VII, *J.*, 1948, 113). In view of the interesting behaviour of the rottlerin derivatives a study of the application of the rottlerone change to a series of analogous symmetrical and unsymmetrical diphenylmethanes, of types (V) and (VI), derived from *C*-methylresorcinol and *C*-methylphloroglucinol has now been made.



By the action of 40% aqueous formaldehyde and alcoholic sulphuric acid on appropriate ketones of the type (I), (II), and (III) the following symmetrical diphenylmethanes were synthesised: (IV; R = Me), (IV; R = Ph), (V; R = Me), (VI; R = Ph, R′ = H), (VI; R = R′ = Me), (VI; R = Ph, R′ = Me), and (VI; R = $Ph{\cdot}CH_2{\cdot}CH_2$, R′ = Me). With the ketones (III; R = Pr^n, R′ = H) and (III; R = $Ph{\cdot}CH_2{\cdot}CH_2$, R′ = H) the use of aqueous formaldehyde gave products consisting mainly of oils along with a little of the required diphenylmethanes, but when paraformaldehyde was employed excellent yields of (VI; R = Pr^n, R′ = H) and (VI; R = $Ph{\cdot}CH_2{\cdot}CH_2$, R′ = H) were obtained. It seems likely that the oils were mixtures of cyclic formals (type VII), which are known to be sometimes formed in the condensation of phenols and formaldehyde with acidic reagents (cf. Borsche and Berkhout,

* Part VII, *J.*, 1948, 113.

Annalen, 1904, **330**, 82; Chattaway and Goepp, *J.*, 1933, 699; Ziegler, *Ber.*, 1941, **74**, 1871). As formaldehyde is liberated very slowly from paraformaldehyde in acid solution, its concentration is small and thus the tendency for the intermediate hydroxybenzyl alcohols to give formals is reduced.

By the procedure employed in the synthesis of tetrahydro- and tetrahydro*allo*-rottlerin a series of unsymmetrical diphenylmethanes was prepared from aqueous formaldehyde or paraformaldehyde and mixtures of the appropriate pairs of ketones, *viz.*, (VIII; R = Ph, R′ = Me), (VIII; R = R′ = Me), (VIII; R = R′ = Ph), (IX; R = Me, R′ = Ph·CH_2·CH_2, R″ = H), (IX; R = Me, R′ = Pr^n, R″ = H), (IX; R = Me, R′ = Ph·CH_2·CH_2, R″ = Me), and (IX; R = Me, R′ = Ph, R″ = Me). As expected, each of these compounds was accompanied by the appropriate pair of symmetrical products. With either of the following pairs of ketones, *viz.*, (I; R = Me) and (I; R = Ph), (II; R = Me) and (II; R = Ph), or (I; R = Ph) and (II; R = Me), (III; R = Me) and (III; R = Ph), or (III; R = Ph) and (III; R = Pr^n), the unsymmetrical product was not formed in quantities detectable by fractional crystallisation and chromatography. Attempts to prepare the hydroxybenzyl alcohols from the last-mentioned ketones by the alkali–formaldehyde method (cf. Lederer and Manasse, *J. pr. Chem.*, 1894, **50**, 223) were unsuccessful and hence it was not possible to prepare the unsymmetrical diphenylmethanes by this route. Similarly, the chloromethyl derivatives (cf. Blanc, *Bull. Soc. chim.*, 1923, **33**, 313, and Sommelet, *ibid.*, 1933, **53**, 853) required for this purpose also could not be obtained.

On being boiled with acetic acid containing a little water, the following unsymmetrical diphenylmethanes derived from resorcinol were slowly converted into the expected pairs of symmetrical compounds, thus

(VIII; R = Ph, R′ = Me) ⟶ (IV; R = Me) + (V; R = Ph)
(VIII; R = R′ = Me) ⟶ (IV; R = Me) + (V; R = Me)
(VIII; R = R′ = Ph) ⟶ (IV; R = Ph) + (V; R = Ph)

but unchanged material invariably remained in each case. When the appropriate pairs of symmetrical diphenylmethanes on the right-hand side above were subjected to the same treatment, the corresponding unsymmetrical products on the left-hand side were formed in small amounts. A comparison of the yields in these reversible reactions indicated that the equilibrium point was not attained during the time of heating (48 hours), whereas with longer treatment the products became more resinous. In the phloroglucinol series the reversible reactions,

(IX; R = Me, R′ = Ph·CH_2·CH_2, R″ = H) ⇌ (VI; R = Me, R′ = H) + (VI; R = Ph·CH_2·CH_2, R′ = H)

and (IX; R = Me, R′ = Pr^n, R″ = H) ⇌ (VI; R = Me, R′ = H) + (VI; R = Pr^n, R′ = H)

proceeded readily and the equilibrium was established in 4 hours. In these cases the disproportionation took place to a slight extent on heating for short periods with solvents used in the purification of these compounds, *e.g.*, alcohol. On the other hand, the reactions,

(IX; R = Me, R′ = Ph·CH_2·CH_2, R″ = Me) ⇌ (VI; R = R′ = Me) + (VI; R = Ph·CH_2·CH_2, R′ = Me)

and (IX; R = Me, R′ = Pr^n, R″ = Me) ⇌ (VI; R = R′ = Me) + (VI; R = Pr^n, R′ = Me),

which were shown to be reversible, were not complete after 15 hours. On being warmed with aqueous acetic acid at 70° for 20 minutes (IX; R = Me, R′ = Ph·CH_2·CH_2, R″ = H) was partly converted into (VI; R = Me, R′ = H) but the second component could not be isolated. This unsymmetrical diphenylmethane also disproportionates in warm dioxan containing hydrochloric acid, giving both symmetrical products.

In general, the results obtained in the foregoing experiments indicate that the unsymmetrical polyhydroxydiphenylmethanes which can be formed from the two requisite symmetrical compounds (*i.e.*, reversing the rottlerone change) are the products which can be synthesised by the application of the phenol–formaldehyde condensation. Conversely, certain unsymmetrical polyhydroxydiphenylmethanes can be prepared neither by the phenol–formaldehyde reaction

nor by the disproportionation method. The disproportionation reaction is clearly a reversible hydrolysis (cf. Granger, *Ind. Eng. Chem.*, 1937, **29**, 1125; Burawoy and Chamberlain, *J.*, 1949, 624, 626) and may be represented thus :

$$(a)\ R{\cdot}CH_2{\cdot}R' + H_2O \rightleftharpoons R{\cdot}CH_2{\cdot}OH + R'H$$
$$(b)\ R{\cdot}CH_2{\cdot}R' + H_2O \rightleftharpoons R'{\cdot}CH_2{\cdot}OH + RH$$
$$(c)\ R{\cdot}CH_2{\cdot}OH + RH \rightleftharpoons R{\cdot}CH_2{\cdot}R + H_2O$$
$$(d)\ R'{\cdot}CH_2{\cdot}OH + R'H \rightleftharpoons R'{\cdot}CH_2{\cdot}R' + H_2O$$

Of the steps (*c*) and (*d*) it is clear that if one is much more rapid than the other the final product of the forward reaction will be almost wholly a symmetrical compound involving the more reactive phenol and the reverse reactions (*c*) and (*d*) will be suppressed. On this view it seemed likely that a polyhydroxydiphenylmethane formed from a less reactive phenol should be completely or almost completely decomposed on being heated with a more reactive phenol, thus : $R{\cdot}CH_2{\cdot}R + 2R'H \longrightarrow R'{\cdot}CH_2{\cdot}R' + 2RH$. In agreement with this it has been found that when the compounds (VI; R = R′ = Me), (VI; R = Ph, R′ = Me), and (VI; R = $Ph{\cdot}CH_2{\cdot}CH_2$, R′ = Me) were each heated with *C*-methylphloracetophenone almost theoretical yields of 5 : 5′-diacetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane (VI; R = Me; R′ = H) were obtained along with the respective less reactive phenols (III; R = R′ = Me), (III; R = Ph, R′ = Me), and (III; R = $Ph{\cdot}CH_2{\cdot}CH_2$, R′ = Me).

The ketones (III; R = $Ph{\cdot}CH_2{\cdot}CH_2$, R′ = Me) and (III; R = Ph, R′ = Me) were prepared from *C*-methylphloroglucinol β-methyl ether and the appropriate nitrile by the Hoesch method. The orientations of these products follow from the fact that on methylation by the methyl iodide–potassium carbonate method they were converted into (X; R = $Ph{\cdot}CH_2{\cdot}CH_2$) and (X; R = Ph) because in this reaction trimethoxy-derivatives would have been formed if the ketone group had been in the *o*-position to the methoxyl group (Curd and Robertson, *J.*, 1933, 437).

Experimental.

5 : 5′-*Diacetyl*-2 : 6 : 2′ : 6′-*tetrahydroxy*-3 : 3′-*dimethyldiphenylmethane* (IV; R = Me).—2 : 4-Dihydroxy-5-methylacetophenone has been prepared from 2 : 4-dihydroxytoluene (Johnson and Lane, *J. Amer. Chem. Soc.*, 1921, **43**, 356) by Yanagita (*Ber.*, 1938, **71**, 2271) by the Nencki reaction, but the Hoesch reaction has been found to give more satisfactory results. Formed by the interaction of the phenol (5 g.), methyl cyanide (4 ml.), zinc chloride (2·5 g.), and excess of hydrogen chloride in ether (40 ml.) during 2 days, the ketimine salt was hydrolysed with boiling water (50 ml.) for ½ hour, and the resulting ketone crystallised from water, forming long, slender, pale yellow needles (4·5 g.), m. p. 169°.

Concentrated sulphuric acid (2 ml.) was added dropwise to a mixture of 2 : 4-dihydroxy-5-methylacetophenone (1 g.), alcohol (10 ml.), and 40% aqueous formaldehyde (2·5 ml.) at 10°, and next day the pale pink crystalline solid was isolated and recrystallised from alcohol, giving 5 : 5′-*diacetyl*-2 : 6 : 2′ : 6′-*tetrahydroxy*-3 : 3′-*dimethyldiphenylmethane* (0·8 g.) in tiny colourless needles, m. p. 258° (decomp.) (Found : C, 66·4; H, 6·0. $C_{19}H_{20}O_6$ requires C, 66·3; H, 5·9%). This compound was sparingly soluble in hot alcohol or acetone, moderately soluble in hot acetic acid, readily soluble in chloroform and benzene, and gave a reddish-brown ferric reaction in alcohol. Prepared by the acetic anhydride–pyridine method, the *tetra-acetate* separated from aqueous alcohol in colourless needles, m. p. 163·5—164° (Found : C, 63·3; H, 5·6. $C_{27}H_{28}O_{10}$ requires C, 63·3; H, 5·5%).

5 : 5′-*Diacetyl*-2 : 4 : 2′ : 4′-*tetrahydroxy*-3 : 3′-*dimethyldiphenylmethane* (V; R = Me).—Concentrated sulphuric acid (2 ml.) was added dropwise to a solution of 2 : 4-dihydroxy-3-methylacetophenone (Rangaswami and Seshadri, *Proc. Indian Acad. Sci.*, 1939, **8**, *A*, 214) (1 g.) in alcohol (5 ml.) and 40% aqueous formaldehyde (2·5 ml.) at room temperature. The product was isolated three days later and, on recrystallisation from aqueous alcohol, gave 5 : 5′-*diacetyl*-2 : 4 : 2′ : 4′-*tetrahydroxy*-3 : 3′-*dimethyldiphenylmethane* in long colourless needles (0·7 g.), m. p. 263—264°, moderately soluble in alcohol, readily soluble in benzene, chloroform, or acetone, and having a purple ferric reaction in alcohol (Found : C, 66·4; H, 5·9%). The *tetra-acetate* formed colourless needles, m. p. 180—181°, from aqueous alcohol (Found : C, 63·5; H, 5·3%).

2 : 4-*Dihydroxy*-5-*methylbenzophenone* (I; R = Ph).—A mixture of 2 : 4-dihydroxytoluene (5 g.), phenyl cyanide (5 ml.), zinc chloride (2·5 g.), and anhydrous ether (30 ml.) was saturated with hydrogen chloride. Three days later the reaction mixture was again saturated with hydrogen chloride and kept for a further 2 days. Hydrolysis of the resulting ketimine salt with boiling water (100 ml.) for 2½ hours gave an oil which slowly solidified. Repeated crystallisation of this from benzene and then water gave 2 : 4-*dihydroxy*-5-*methylbenzophenone* in pale yellow needles (6 g.), m. p. 137·5—138°, soluble in alcohol, sparingly soluble in cold benzene or cold water, and having a brownish-red ferric reaction in alcohol (Found : C, 73·6; H, 5·5. $C_{14}H_{12}O_3$ requires C, 73·7; H, 5·3%). The *diacetate* separated from dilute alcohol in long colourless needles, m. p. 88—89° (Found : C, 69·5; H, 5·3. $C_{17}H_{16}O_5$ requires C, 69·2; H, 5·2%). The 2 : 4-*dinitrophenylhydrazone* formed dark red needles, m. p. 259° (decomp.), from alcohol (Found : N, 13·6. $C_{26}H_{16}O_6N_4$ requires N, 13·7%).

5 : 5′-*Dibenzoyl*-2 : 6 : 2′ : 6′-*tetrahydroxy*-3 : 3′-*dimethyldiphenylmethane* (IV; R = Ph).—The interaction of the foregoing ketone (1 g.) in alcohol (10 ml.), 40% aqueous formaldehyde (2·5 ml.), and concentrated sulphuric acid (2 ml.) at room temperature during 24 hours gave 5 : 5′-*dibenzoyl*-2 : 6 : 2′ : 6′-*tetrahydroxy*-3 : 3′-*dimethyldiphenylmethane*, which separated from alcohol in pale yellow needles (0·75 g.), m. p. 240°, sparingly soluble in hot alcohol or hot acetone, readily soluble in benzene or chloroform, and having a reddish-brown ferric reaction in alcohol (Found: C, 74·2; H, 5·3. $C_{29}H_{24}O_8$ requires C, 74·4; H, 5·2%). The *tetra-acetate* formed colourless needles, m. p. 184—185°, from aqueous alcohol (Found: C, 69·7; H, 5·3. $C_{37}H_{32}O_{16}$ requires C, 69·8; H, 5·1%).

5 : 5′-*Dibenzoyl*-2 : 4 : 2′ : 4′-*tetrahydroxy*-3 : 3′-*dimethyldiphenylmethane* (V; R = Ph) was prepared from 2 : 4-dihydroxy-3-methylbenzophenone (Jones and Robertson, *J.*, 1932, 1693) (1 g.), 40% aqueous formaldehyde (2·5 ml.), and sulphuric acid (2 ml.) in alcohol (5 ml.) during 3 days and formed small yellow cubes (0·7 g.), m. p. 207—208°, from 80% alcohol, readily soluble in chloroform, benzene, hot alcohol or hot acetic acid and having a reddish-brown ferric reaction in alcohol (Found: C, 74·1; H, 5·4%). The *tetra-acetate* crystallised from aqueous alcohol in tiny colourless needles, m. p. 176—177° (Found: C, 70·0; H, 5·2%).

5 : 5′-*Dibenzoyl*-2 : 4 : 2′ : 6′-*tetrahydroxy*-3 : 3′-*dimethyldiphenylmethane* (VIII; R = R′ = Ph).—Concentrated sulphuric acid (2 ml.) was added dropwise to a solution of 2 : 4-dihydroxy-3-methylbenzophenone (0·5 g.) and 2 : 4-dihydroxy-5-methylbenzophenone (0·5 g.) in alcohol (7 ml.) containing 40% aqueous formaldehyde (2·5 ml.), and 7 days later the mixed product (0·7 g.) was collected, washed well with water, and extracted with boiling 80% alcohol. Crystallisation of the residue (0·2 g.), m. p. 204°, from alcohol gave 5 : 5′-dibenzoyl-2 : 6 : 2′ : 6′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane (IV; R = Ph), m. p. and mixed m. p. 238—240°. The cooled alcoholic extract deposited 5 : 5′-*dibenzoyl*-2 : 4 : 2′ : 6′-*tetrahydroxy*-3 : 3′-*dimethyldiphenylmethane* in yellow needles (0·2 g.), m. p. 219—224°, which on recrystallisation from 95% alcohol had m. p. 222—224°, and gave a reddish-brown ferric reaction (Found: C, 74·1; H, 5·3%). Prepared by the pyridine method during 7 days, the *acetate* formed clusters of colourless needles, m. p. 189—191°, from alcohol (Found: C, 69·8; H, 5·3%). On admixture with its 2 : 4 : 2′ : 4′-tetrahydroxy-isomer, this compound had m. p. 186—188°, and with its 2 : 6 : 2′ : 6′-tetrahydroxy-isomer had m. p. 203—206°.

On being diluted with water (5 ml.) the original extract left after the isolation of 5 : 5′-dibenzoyl-2 : 4 : 2′ : 6′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane deposited a solid (0·3 g.) which on recrystallisation from 70% alcohol gave 5 : 5′-dibenzoyl-2 : 4 : 2′ : 4′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane (V; R = Ph), m. p. and mixed m. p. 205—207°.

5-*Acetyl*-5′-*benzoyl*-2 : 4 : 2′ : 6′-*tetrahydroxy*-3 : 3′-*dimethyldiphenylmethane* (VIII; R = Ph, R′ = Me).—The interaction of 2 : 4-dihydroxy-5-methylacetophenone (0·5 g.), 2 : 4-dihydroxy-3-methylbenzophenone (0·5 g.) in alcohol (10 ml.), 40% aqueous formaldehyde (2·5 ml.), and concentrated sulphuric acid (2 ml.; added dropwise) during 3 days gave a mixture (0·7 g.) which was extracted with boiling alcohol (2 × 20 ml.). Crystallisation of the insoluble residue (0·22 g.), m. p. *ca.* 210°, from alcohol, gave 5 : 5′-diacetyl-2 : 6 : 2′ : 6′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane (IV; R = Me), m. p. 258° (decomp.). On being kept the combined extracts deposited a product in yellow needles (0·28 g.), m. p. 228—235° which, on being recrystallised twice from alcohol, furnished 5-*acetyl*-5′-*benzoyl*-2 : 4 : 2′ : 6′-*tetrahydroxy*-3 : 3′-*dimethyldiphenylmethane* in pale yellow needles, m. p. 239—240°, moderately soluble in hot alcohol and having a brownish-red ferric reaction in alcohol (Found: C, 71·1; H, 5·5. $C_{24}H_{22}O_8$ requires C, 70·9; H, 5·5%). Admixed with its 5 : 5′-diacetyl-2 : 6 : 2′ : 6′-tetrahydroxy-analogue this compound had m. p. 190—200°, and with 5 : 5′-dibenzoyl-2 : 4 : 2′ : 4′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane had m. p. *ca.* 180°.

Prepared by the pyridine method in the course of 10 days the *tetra-acetate* crystallised from aqueous alcohol in clusters of rectangular plates, m. p. 150—151° (Found: C, 66·8; H, 5·4. $C_{32}H_{30}O_{10}$ requires C, 66·9; H, 5·3%).

After the isolation of the crude 5-acetyl-5′-benzoyl-2 : 6 : 2′ : 6′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane, dilution of the extract with water (100 ml.) gave a flocculent precipitate (0·2 g.), m. p. *ca.* 160°, from which a small quantitiy of 5 : 5′-dibenzoyl-2 : 4 : 2′ : 4′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane (V; R = Ph), m. p. 207—208°, was isolated by recrystallisation (4 times) from alcohol.

5 : 5′-*Diacetyl*-2 : 4 : 2′ : 6′-*tetrahydroxy*-3 : 3′-*dimethyldiphenylmethane* (VIII; R = R′ = Me).—The mixed product (0·85 g.) from the interaction of 2 : 4-dihydroxy-3-methylacetophenone (0·5 g.), 2 : 4-dihydroxy-5-methylacetophenone (0·5 g.), 40% aqueous formaldehyde (2·5 g.), and concentrated sulphuric acid (2 ml.) in alcohol (10 ml.) during 4 days was triturated with boiling alcohol (10 ml.), leaving a colourless residue (0·2 g.) of slightly impure 5 : 5′-diacetyl-2 : 6 : 2′ : 6′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane, m. p. 255°. On cooling, the alcoholic liquor deposited a pinkish solid, m. p. 224°, which on purification from alcohol gave 5 : 5′-*diacetyl*-2 : 4 : 2′ : 6′-*tetrahydroxy*-3 : 3′-*dimethyldiphenylmethane* in colourless needles (0·3 g.), m. p. 237—239° (decomp.), readily soluble in hot acetic acid or benzene and having a red-violet ferric reaction in alcohol (Found: C, 66·6; H, 6·1. $C_{19}H_{20}O_8$ requires C, 66·3; H, 5·9%). Mixtures of this compound and 5 : 5′-diacetyl-2 : 4 : 2′ : 4′- and 5 : 5′-diacetyl-2 : 6 : 2′ : 6′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane had m. p. *ca.* 220° and m. p. *ca.* 231°, respectively. The *tetra-acetate* formed colourless needles, m. p. 171—172° (Found: C, 63·2; H, 5·7. $C_{27}H_{28}O_{10}$ requires C, 63·3; H, 5·5%).

Dilution of the residual alcoholic extract with water (50 ml.) furnished a flocculent precipitate which was crystallised 3 times from alcohol, giving 5 : 5′-diacetyl-2 : 4 : 2′ : 4′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane (0·15 g.), m. p. and mixed m. p. 263—264°.

Disproportionation of 5 : 5′-*Diacetyl*-2 : 4 : 2′ : 6′-*tetrahydroxy*-3 : 3′-*dimethyldiphenylmethane* (VIII; R = R′ = Me).—A solution of this compound (0·7 g.) in acetic acid (40 ml.) and water (5 ml.) was heated under reflux for 48 hours, the greater part of the solvent was evaporated in a vacuum, and the residue

was diluted with water (50 ml.). Next day the resulting light brown solid (0·6 g.) was extracted with boiling alcohol (2 × 20 ml.), and the residue (0·075 g.), m. p. 240°, crystallised from alcohol (charcoal), giving 5 : 5′-diacetyl-2 : 6 : 2′ : 6′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane (IV; R = Me) in tiny, almost colourless needles, m. p. 258° (decomp.). On recrystallisation the pale pink solid (0·42 g.), m. p. 220° (approx.), deposited by the cooled alcoholic extracts gave unchanged 5 : 5′-diacetyl-2 : 4 : 2′ : 6′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane, m. p. and mixed m. p. 236—239° (decomp.). After the separation of this product the extracts were diluted with water (100 ml.), giving a somewhat resinous precipitate (0·09 g.) which, on recrystallisation from aqueous acetic acid and then alcohol (charcoal), furnished a small amount of 5 : 5′-diacetyl-2 : 4 : 2′ : 4′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane (V; R = Me), m. p. and mixed m. p. 263—264°.

A mixture of 5 : 5′-diacetyl-2 : 4 : 2′ : 4′-tetrahydroxy- (V; R = Me) (0·5 g.) and 5 : 5′-diacetyl-2 : 6 : 2′ : 6′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane (IV; R = Me) (0·5 g.), acetic acid (50 ml.), and water (5 ml.) was heated under reflux for 48 hours, the solvent was evaporated in a vacuum, and the light brown solid, m. p. *ca.* 160—180°, was extracted with boiling alcohol (50 ml.), leaving a residue (0·35 g.) which, on recrystallisation from alcohol (charcoal), gave unchanged 5 : 5′-diacetyl-2 : 6 : 2′ : 6′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane, m. p. 258° (decomp.). The alcoholic extract deposited light pink needles (0·12 g.), m. p. 190—200°, consisting of 5 : 5′-diacetyl-2 : 4 : 2′ : 6′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane (VIII; R = R′ = Me) mixed with a little unchanged 2 : 4 : 2′ : 4′-tetrahydroxy-compound which was removed by recrystallisation from hot alcohol. The extract was then evaporated to a small volume and diluted with water (5 ml.), giving a somewhat resinous solid (0·3 g.) from which a small amount of unchanged 5 : 5′-diacetyl-2 : 4 : 2′ : 4′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane was obtained by crystallisation from alcohol.

Disproportionation of 5′-Acetyl-5-benzoyl-2 : 4 : 2′ : 6′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane (VIII; R = Ph, R′ = Me).—This compound (0·75 g.) was heated under reflux with acetic acid (40 ml.) and water (5 ml.) for 48 hours. The product left on distillation of the solvent was separated into 5 : 5′-diacetyl-2 : 6 : 2′ : 6′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane (IV; R = Me), m. p. 258° (decomp.), unchanged 5′-acetyl-5-benzoyl-2 : 4 : 2′ : 6′-tetrahydroxy-3 : 3′dimethyldiphenylmethane (0·32 g.), m. p. 239°, and 5 : 5′-dibenzoyl-2 : 4 : 2′ : 4′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane (V; R = Ph), m. p. 207—208°, by the procedure employed in the case of 5 : 5′-diacetyl-2 : 4 : 2′ : 6′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane.

A solution of 5 : 5′-dibenzoyl-2 : 4 : 2′ : 4′-tetrahydroxy- (0·5 g.) and 5 : 5′-diacetyl-2 : 6 : 2′ : 6′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane (0·5 g.) in acetic acid (50 ml.) and water (3 ml.) was heated under reflux for 48 hours, evaporated to small volume, and diluted with water (50 ml.). The solid (0·85 g.) was separated into 5 : 5′-diacetyl-2 : 6 : 2′ : 6′-tetrahydroxy- (0·41 g.), 5′-acetyl-5-benzoyl-2 : 4 : 2′ : 6′-tetrahydroxy- (0·11 g.), and 5 : 5′-dibenzoyl-2 : 4 : 2′ : 4′-tetrahydroxy-3 : 3′-dimethyldiphenylmethane (small quantity).

C-Methylphloroglucinol.—Phloroglucinolaldehyde dihydrate (5 g.), dissolved in ethyl acetate (100 ml.), was reduced with a Raney nickel catalyst (Parlic and Adkins, *J. Amer. Chem. Soc.*, 1946, **68**, 1471) (10 g. of moist catalyst) and hydrogen at 65 lb./sq. in. during 15 hours. After the removal of the catalyst, which was well washed with ethyl acetate, the solution was concentrated in a vacuum and the solid was dried and recrystallised from ethyl acetate–light petroleum, giving *C*-methylphloroglucinol in tiny colourless needles, m. p. 213—215° (yield, 3·2 g., 96%)

Applied to 2 : 4-dihydroxy-6-methoxybenzaldehyde, the same procedure afforded a much more convenient route to *C*-methylphloroglucinol β-methyl ether than either the method of Herzig and Wenzel (*Monatsh.*, 1902, **23**, 80) or that of Curd and Robertson (*J.*, 1933, 1179). Under the same conditions the reduction of this aldehyde (Head and Robertson, *J.*, 1930, 2440) was complete in 4 hours and gave *C*-methylphloroglucinol β-methyl ether, forming colourless prisms (4·3 g.), m. p. 117—119°, from benzene.

2 : 4 : 6-*Trihydroxy-3-methyl-β-phenylpropiophenone.*—Formed by the condensation of *C*-methylphloroglucinol (4·5 g.) and β-phenylpropionitrile (Henley and Turner, *J.*, 1931, 1183) (6 ml.) in ether (150 ml.) with zinc chloride (2 g.) and an excess of hydrogen chloride during 24 hours, the semi-solid ketimine salt was dissolved in water (100 ml.), and the solution (almost neutralised with sodium hydrogen carbonate) heated under reflux for 2 hours. On cooling, the resulting dark oil solidified and on crystallisation from benzene and then from water gave 2 : 4 : 6-trihydroxy-3-methyl-β-phenylpropiophenone as the *monohydrate* (2·9 g.) in almost colourless lustrous needles, m. p. 138° (Found: H_2O, 6·6. $C_{16}H_{16}O_4.H_2O$ requires H_2O, 6·3%). The anhydrous *ketone* had m. p. 173—174° (Found: C, 70·4; H, 6·0. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%). This compound, which was readily soluble in alcohol and moderately soluble in hot water, gave a violet ferric reaction in alcohol.

Warmed for 3 minutes with alcoholic diazoaminobenzene, the ketone gave 2 : 4 : 6-*trihydroxy-3-methyl-5-β-phenylpropionylazobenzene*, which formed scarlet needles, m. p. 182—183°, from 95% acetic acid (Found: C, 70·4; H, 5·5; N, 7·5. $C_{22}H_{20}O_4N_2$ requires C, 70·2; H, 5·4; N, 7·5%). Methylation of this ketone (0·5 g.) with methyl iodide (4 ml.) and potassium carbonate (6 g.) in boiling acetone (20 ml.) for 4 hours, with the addition of more iodide (3 ml.) and carbonate (6 g.) after 2 hours, gave 6-*hydroxy-2 : 4-dimethoxy-3-methyl-β-phenylpropiophenone*, which formed colourless needles (0·4 g.), m. p. 144—145°, from alcohol, soluble in dilute aqueous sodium hydroxide and giving a green ferric reaction in alcohol [Found: C, 63·9; H, 4·9; OMe, 20·8. $C_{16}H_{14}O_3(OMe)_2$ requires C, 64·0; H, 4·7; OMe, 20·7%].

2 : 4 : 6 : 2′ : 4′ : 6′-*Hexahydroxy-3 : 3′-dimethyl-5 : 5′-di-β-phenylpropionyldiphenylmethane* (IX; R = R′ = $Ph{\cdot}CH_2{\cdot}CH_2$, R″ = H).—A mixture of 2 : 4 : 6-trihydroxy-3-methyl-β-phenylpropiophenone (0·5 g.), powdered paraformaldehyde (0·2 g.), concentrated sulphuric acid (7 drops), and alcohol (10 ml.) was gently agitated for 48 hours, and the light pink product crystallised from alcohol (charcoal), giving 2 : 4 : 6 : 2′ : 4′ : 6′-*hexahydroxy-3 : 3′-dimethyl-5 : 5′-di-β-phenylpropionyldiphenylmethane* in pale yellow needles (0·4 g.), m. p. 203—205°, soluble in hot alcohol, sparingly soluble in benzene, and having a

brownish-green ferric reaction in alcohol (Found: C, 71·1; H, 6·0. $C_{33}H_{32}O_8$ requires C, 71·2; H, 5·8%). Attempts to acetylate or to methylate this compound gave intractable products. Interaction of this diphenylmethane (0·5 g.) with diazoaminobenzene (0·5 g.) in alcohol (5 ml.) on the steam-bath for 5 minutes yielded 2 : 4 : 6-trihydroxy-3-methyl-5-β-phenylpropionylazobenzene, m. p. and mixed m. p. 182—183°, after recrystallisation.

5-Acetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-5′-β-phenylpropionyldiphenylmethane (IX; R = Me, R′ = Ph·CH_2·CH_2, R″ = H).—A mixture of 2 : 4 : 6-trihydroxy-3-methylacetophenone (Curd and Robertson, *J.*, 1933, 441) (0·5 g.) and 2 : 4 : 6-trihydroxy-3-methyl-β-phenylpropiophenone (0·75 g.), paraformaldehyde (0·4 g.), concentrated sulphuric acid (10 drops), and alcohol (10 ml.) was agitated gently for 48 hours, and water (4 ml.) then added to complete the separation of the product which on isolation was washed with water to remove acid and then extracted with hot 85% acetone (35 ml.). On crystallisation from aqueous dioxan the residual solid (0·25 g.), m. p. 270—280°, gave 5 : 5′-diacetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane, m. p. 291° (decomp.), identical with an authentic specimen (McGookin *et al.*, *J.*, 1939, 1585). Spontaneous evaporation of the aqueous acetone extract to about half its volume furnished an orange-yellow solid, m. p. 250—258° (0·4 g.), which on purification 3 times from aqueous acetone gave *5-acetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyl-5′-β-phenylpropionyldiphenylmethane* in microscopic, light yellow needles, m. p. 258—260° (decomp.), moderately soluble in acetone or hot alcohol and giving a red-brown ferric reaction in alcohol (Found: C, 66·8; H, 6·0. $C_{26}H_{26}O_8$ requires C, 66·9; H, 5·6%). Warmed with a solution of diazoaminobenzene (0·4 g.) in alcohol (7 ml.) on the steam-bath for 5 minutes this diphenylmethane (0·4 g.) gave 5-acetyl-2 : 4 : 6-trihydroxy-3-methylazobenzene, m. p. 202°, identical with an authentic specimen. A second crystalline azo-derivative could be isolated.

Evaporation of the acetone extract left after the separation of 5-acetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-5′-β-phenylpropionyldiphenylmethane gave 2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyl-5 : 5′-di-β-phenylpropionyldiphenylmethane, m. p. and mixed m. p. 203—205°, after repeated purification from alcohol.

Disproportionation of 5-Acetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyl-5′-β-phenylpropionyldiphenylmethane (IX; R = Me, R′ = Ph·CH_2·CH_2, R″ = H).—(*a*) A solution of this compound (0·75 g.) in acetic acid (40 ml.) and water (5 ml.) was gently heated under reflux for 6 hours and then filtered to remove solid (0·18 g.), m. p. about 270°, which, on recrystallisation from aqueous dioxan, gave 5 : 5′-diacetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane (IX; R = R′ = Me, R″ = H), m. p. 290°. The acetic acid liquor was concentrated in a vacuum and diluted with water (30 ml.), and the solid (0·45 g.) separated by slow crystallisation from cold acetone (50 ml.) into unchanged 5-acetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-5′-β-phenylpropionyldiphenylmethane (0·32 g.), m. p. approx. 250°, which on purification had m. p. 258—260°, and a somewhat resinous product (0·1 g.), which, on crystallisation from aqueous alcohol (charcoal) 3 times, gave a little 2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyl-5 : 5′-di-β-phenylpropionyldiphenylmethane (IX; R = R′ = Ph·CH_2·CH_2, R″ = H), m. p. and mixed m. p. 202—205°.

A mixture of 5 : 5′-diacetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane (0·4 g.), 2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyl-5 : 5′-di-β-phenylpropionyldiphenylmethane (0·55 g.), acetic acid (45 ml.), and water (5 ml.) was gently heated under reflux for 6 hours and then filtered to remove unchanged 5 : 5′-diacetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane (0·25 g.), m. p. *ca.* 275°, which on purification had m. p. 288°. On evaporation in a vacuum the filtrate yielded a resinous solid (0·65 g.), m. p. approx. 180°, which was separated as above into a little 2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyl-5 : 5′-di-β-phenylpropionyldiphenylmethane and slightly impure 5-acetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyl-5′-β-phenylpropionyldiphenylmethane (0·4 g.), m. p. 254°.

(*b*) A solution of 5-acetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyl-5′-β-phenylpropionyldiphenylmethane (0·5 g.) in 2N-aqueous sodium carbonate (30 ml.) was kept at 70° for 20 minutes, cooled, and acidified with dilute hydrochloric acid. The precipitate (0·4 g.) was extracted with a hot mixture of acetone (20 ml.) and water (5 ml.), and the residue (0·09 g.) crystallised from aqueous dioxan, giving 5 : 5′-diacetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane, m. p. 291° (decomp.). Evaporation of the acetone extract gave unchanged 5-acetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyl-5′-β-phenylpropionyldiphenylmethane (0·25 g.) and a resinous product from which a definite compound could not be obtained.

(*c*) A mixture of 5-acetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyl-5′-β-phenylpropionyldiphenylmethane (0·5 g.), dioxan (15 ml.), and concentrated hydrochloric acid (0·5 g.) was heated under reflux for ½ hour and evaporated in a vacuum, leaving a brown-yellow solid which was separated by means of dilute acetone into impure 5 : 5′-diacetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane (0·09 g.), m. p. 288—291°, unchanged 5-acetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyl-5′-β-phenylpropionyldiphenylmethane (0·25 g.), m. p. 258—260° (decomp.), and an amorphous residue.

5 : 5′-Di-n-butyryl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane (IX; R = R′ = Pr^n, R″ = H).—Karrer's method (*Helv. Chim. Acta*, 1919, **2**, 481) was found to give poor yields of this compound, and the condensation of 2 : 4 : 6-trihydroxy-3-methyl-*n*-butyrophenone (Karrer, *loc. cit.*) with 40% aqueous formaldehyde by either concentrated sulphuric acid or hydrochloric acid gave a small yield of a resinous product.

A mixture of 2 : 4 : 6-trihydroxy-3-methyl-*n*-butyrophenone (0·5 g.) in methanol (7 ml.) and water (2 ml.), paraformaldehyde (0·15 g.), and concentrated sulphuric acid (10 drops) was agitated for 24 hours. The precipitate consisted of 5 : 5′-di-*n*-butyryl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane, forming tiny pale yellow needles (0·45 g.), m. p. 212° from alcohol, which gave resinous products on acetylation or methylation.

5-Acetyl-5′-n-butyryl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane (IX; R = Me, R′ = Pr^n, R″ = H).—A mixture of 2 : 4 : 6-trihydroxy-3-methyl-*n*-butyrophenone (0·5 g.) and 2 : 4 : 6-trihydroxy-3-methylacetophenone (0·5 g.), alcohol (10 ml.), water (3 ml.), paraformaldehyde (0·25 g.), and concentrated sulphuric acid (10 drops) was agitated for 48 hours, and the solid (0·8 g.) washed with water and extracted with a mixture of hot 85% acetone (35 ml.), leaving a residue (0·32 g.) of 5 : 5′-diacetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane, m. p. 265—270°, which on purification from hot dioxan had m. p. 289—291° (decomp.). Evaporation of the acetone extract gave a solid (0·15 g.), m. p. 242—246°, which on being thrice crystallised from aqueous acetone furnished *5-acetyl-5′-n-butyryl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane* in very pale yellow needles, m. p. 246—248°, moderately soluble in hot alcohol, and having a bright red ferric reaction in alcohol (Found : C, 62·0; H, 6·0. $C_{21}H_{24}O_8$ requires C, 62·4; H, 6·0%). After the removal of this compound 5 : 5′-di-*n*-butyryl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane (0·25 g.) was isolated.

Disproportionation of 5-Acetyl-5′-n-butyryl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane.—This compound (0·5 g.) was heated under reflux with acetic acid (25 ml.) and water (2 ml.) for 5 hours and the hot mixture filtered to remove 5 : 5′-diacetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane (IX; R = Me, R′ = H) (0·17 g.), m. p. 270°. The solid obtained by evaporation of the acidic liquor gave unchanged 5-acetyl-5′-*n*-butyryl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane (0·09 g.) and a small amount of 5 : 5′-di-*n*-butyryl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane.

A mixture of 5 : 5′-diacetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane (0·4 g.) and 5 : 5′-di-*n*-butyryl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane (0·5 g.), acetic acid (40 ml.), and water (5 ml.) was gently heated under reflux for 5 hours, giving unchanged material (0·3 g.), 5-acetyl-5′-*n*-butyryl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane (0·14 g.), and a small amount of the 5 : 5′-di-*n*-butyryl compound.

2 : 4 : 6-Trihydroxy-3-methylbenzophenone.—The condensation of *C*-methylphloroglucinol (5 g.) and phenyl cyanide (6 ml.) in ether (150 ml.) by means of zinc chloride (2 g.) and excess of hydrogen chloride yielded a dark viscous oil which on hydrolysis with boiling water (100 ml.) for 75 minutes gave a semi-solid. Crystallised from hot 2N-sulphuric acid and then hot water (charcoal), this product gave *2 : 4 : 6-trihydroxy-3-methylbenzophenone* in yellow rhombic plates (4·5 g.), m. p. 139—140°, moderately soluble in hot water, readily soluble in alcohol, and giving a dark red ferric reaction in alcohol (Found : C, 68·7; H, 5·1. $C_{14}H_{12}O_4$ requires C, 68·9; H, 5·0%). The *triacetate* separated from aqueous alcohol in colourless plates, m. p. 112—113° (Found : C, 64·5; H, 4·6. $C_{20}H_{18}O_7$ requires C, 64·8; H, 4·9%). Interaction of the ketone with warm alcoholic diazoaminobenzene for 3 minutes gave *3-benzoyl-2 : 4 : 6-trihydroxy-5-methylazobenzene*, which formed red, crescent-shaped needles, m. p. 184—185°, from acetic acid (Found : C, 68·9; H, 4·9. $C_{20}H_{16}O_4N_2$ requires C, 69·0; H, 4·6%).

Methylation of this ketone by the methyl iodide–potassium carbonate method gave *2-hydroxy-4 : 6-dimethoxy-3-methylbenzophenone*, which formed lustrous, almost colourless plates, m. p. 136—137°, from dilute alcohol, soluble in dilute aqueous sodium hydroxide and having a violet ferric reaction in alcohol (Found : C, 70·5; H, 6·0; OMe, 20·9. $C_{16}H_{16}O_4$ requires C, 70·6; H, 6·0; OMe, 22·8%).

5 : 5′-Dibenzoyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane (IX; R = R′ = Ph, R″ = H) was prepared from 2 : 4 : 6-trihydroxy-3-methylbenzophenone (1 g.), 40% aqueous formaldehyde (2 ml.), and alcohol (15 ml.) containing concentrated sulphuric acid (15 drops) in the course of 24 hours and formed yellow needles (0·8 g.), m. p. 242—243°, from dilute alcohol, readily soluble in alcohol and having a red-brown ferric reaction (Found : C, 69·4; H, 5·0. $C_{28}H_{24}O_8$ requires C, 69·6; H, 4·9%). The *hexa-acetate* separated from dilute alcohol in colourless rhombic plates, m. p. 136—138° (Found : C, 65·2; H, 5·0. $C_{41}H_{36}O_{14}$ requires C, 65·4; H, 4·8%). Methylation of this diphenylmethane by the methyl sulphate–potassium carbonate method during 4 hours gave the *hexamethyl ether*, which separated from light petroleum (b. p. 40—60°) and then aqueous alcohol in colourless needles, m. p. 168—169° [Found : C, 71·9; H, 6·3; OMe, 32·5. $C_{28}H_{18}O_2(OMe)_6$ requires C, 71·9; H, 6·2; OMe, 31·9%].

3 : 3′-Diacetyl-2 : 4 : 2′ : 4′-tetrahydroxy-6 : 6′-dimethoxy-5 : 5′-dimethyldiphenylmethane (IX; R = R′ = R″ = Me) was prepared from 2 : 6-dihydroxy-4-methoxy-3-methylacetophenone (Curd and Robertson, *J.*, 1933, 1179) (1 g.) by the formaldehyde–sulphuric acid method and on isolation formed very pale yellow prisms (0·8 g.), m. p. 218—219° (decomp.), from alcohol, having a green ferric reaction in alcohol [Found : C, 62·4; H, 6·2; OMe, 15·1. $C_{15}H_{18}O_6(OMe)_2$ requires C, 62·4; H, 6·0; OMe, 15·3%]. The hexamethyl ether had m. p. 102—103°, and was identical with an authentic specimen (McGookin *et al.*, *J.*, 1939, 1585). The *tetra-acetate* formed squat prisms, m. p. 146—147°, from aqueous alcohol (Found : C, 61·0; H, 5·8. $C_{32}H_{32}O_{12}$ requires C, 60·8; H, 5·6%).

2 : 6-Dihydroxy-4-methoxy-3-methyl-β-phenylpropiophenone.—The condensation of *C*-methylphloroglucinol β-methyl ether (3·8 g.) and β-phenylpropionitrile (4 ml.) by Hoesch's method gave a viscous product which on hydrolysis with boiling water (100 ml.) for ½ hour furnished *2 : 6-dihydroxy-4-methoxy-3-methyl-β-phenylpropiophenone*. This ketone separated from alcohol in lustrous yellow plates (2 g.), m. p. 172—173°, moderately soluble in hot benzene, sparingly soluble in hot water, and giving a dark violet ferric reaction in alcohol (Found : C, 71·2; H, 6·5. $C_{17}H_{18}O_4$ requires C, 71·4; H, 6·4%). The *2 : 4-dinitrophenylhydrazone* formed scarlet needles, m. p. 212—214°, from ethyl acetate–light petroleum (b. p. 60—80°) (Found : N, 12·2. $C_{23}H_{22}O_7N_4$ requires N, 12·0%), and the *diacetate* colourless rhombic plates, m. p. 75—76°, from dilute alcohol (Found : C, 68·2; H, 6·2; OMe, 8·2. $C_{20}H_{18}O_5$·OMe requires C, 68·1; H, 6·0; OMe, 8·4%).

Methylation of this ketone by the methyl iodide–potassium carbonate method furnished 2-hydroxy-4 : 6-dimethoxy-3-methyl-β-phenylpropiophenone, m. p. 144—145·5°, identical with an authentic specimen.

2 : 4 : 2′ : 4′-*Tetrahydroxy*-6 : 6′-*dimethoxy*-3 : 3′-*di*-β-*phenylpropionyl*-5 : 5′-*dimethyldiphenylmethane* (IX; R = R′ = Ph·CH_2·CH_2, R″ = Me) was prepared from 2 : 6-dihydroxy-4-methoxy-3-methyl-β-phenylpropiophenone by the formaldehyde–sulphuric acid method and separated from alcohol in lustrous pale yellow plates, m. p. 171—172°, readily soluble in hot acetic acid and having a green ferric reaction in alcohol [Found : C, 71·7; H, 6·4; OMe, 10·6. $C_{32}H_{30}O_6(OMe)_2$ requires C, 71·9; H, 6·2; OMe, 10·6%]. The *tetra-acetate* formed colourless prisms, m. p. 114—115°, from ethyl acetate–light petroleum (Found : C, 68·3; H, 6·1. $C_{48}H_{44}O_{13}$ requires C, 68·6; H, 5·9%).

3-*Acetyl*-2 : 4 : 2′ : 4′-*tetrahydroxy*-6 : 6′-*dimethoxy*-3′-β-*phenylpropionyl*-5 : 5′-*dimethyldiphenylmethane* (IX; R = Me, R′ = Ph·CH_2·CH_2, R″ = Me).—The interaction of 2 : 6-dihydroxy-5-methoxy-3-methyl-β-phenylpropiophenone (0·75 g.), 2 : 6-dihydroxy-4-methoxy-3-methylacetophenone (0·5 g.), 40% aqueous formaldehyde (2·5 ml.), and concentrated sulphuric acid (15 drops) in alcohol (10 ml.) during two days gave a mixed product (1 g.) which was separated by fractional crystallisation from alcohol into 2 : 4 : 2′ : 4′-tetrahydroxy-6 : 6′-dimethoxy-5 : 5′-dimethyl-3 : 3′-di-β-phenylpropionyldiphenylmethane (0·3 g.), m. p. and mixed m. p. 171—172°, 3-*acetyl*-2 : 4 : 2′ : 4′-*tetrahydroxy*-6 : 6′-*dimethoxy*-5 : 5′-*dimethyl*-3′-β-*phenylpropionyldiphenylmethane* in almost colourless needles, m. p. 189—191°, from alcohol, having a green ferric reaction [Found : C, 68·0; H, 6·2; OMe, 12·8. $C_{26}H_{24}O_6(OMe)_2$ requires C, 68·0; H, 6·1; OMe, 12·6%], and a small amount of 3 : 3′-diacetyl-2 : 4 : 2′ : 4′-tetrahydroxy-6 : 6′-dimethoxy-5 : 5′-dimethylphenylmethane, m. p. 216—219°.

Disproportionation of 3-acetyl-2 : 4 : 2′ : 4′-tetrahydroxy-6 : 6′-dimethoxy-5 : 5′-dimethyl-3′-β-phenylpropionyldiphenylmethane (0·6 g.) in boiling acetic acid (30 ml., containing 2 ml. of water) for 15 hours gave a brownish-yellow solid of indefinite m. p. which on fractional crystallisation from alcohol was resolved into 2 : 4 : 2′ : 4′-tetrahydroxy-6 : 6′-dimethoxy-5 : 5′-dimethyl-3 : 3′-di-β-phenylpropionyldiphenylmethane (0·15 g.), m. p. 170—172°, unchanged 3-acetyl-2 : 4 : 2′ : 4′-tetrahydroxy-6 : 6′-dimethoxy-5 : 5′-dimethyl-3′-β-phenylpropionyldiphenylmethane (0·2 g.), and a small amount of 3 : 3′-diacetyl-2 : 4 : 2′ : 4′-tetrahydroxy-6 : 6′-dimethoxy-5 : 5′-dimethyldiphenylmethane, m. p. 217—219°.

2 : 6-*Dihydroxy*-4-*methoxy*-3-*methylbenzophenone* was prepared from *C*-methylphloroglucinol β-methyl ether (3 g.) and phenyl cyanide (3 ml.) by Hoesch's method and on crystallisation from benzene and then aqueous alcohol formed lustrous bright yellow prisms (2·5 g.), m. p. 143—144°, moderately soluble in alcohol, sparingly soluble in hot water, and having a reddish-brown ferric reaction (Found : C, 69·7; H, 5·6; OMe, 10·7. $C_{14}H_{11}O_5$·OMe requires C, 69·8; H, 5·5; OMe, 12·0%). The 2 : 4-*dinitrophenylhydrazone* separated from acetic acid in orange-red needles, m. p. 215—216° (Found : N, 12·6. $C_{21}H_{18}O_7N_4$ requires N, 12·6%), and the *diacetate* from aqueous alcohol in colourless rhombic prisms, m. p. 134—135° (Found : C, 66·7; H, 5·3. $C_{19}H_{18}O_6$ requires C, 66·7; H, 5·3%).

On methylation by the methyl iodide–potassium carbonate method for 8 hours this ketone gave 2-hydroxy-4 : 6-dimethoxy-3-methylbenzophenone, m. p. and mixed m. p. 136—137°, after purification.

3 : 3′-*Dibenzoyl*-2 : 4 : 2′ : 4′-*tetrahydroxy*-6 : 6′-*dimethoxy*-5 : 5′-*dimethyldiphenylmethane* (IX; R = R′ = Ph, R″ = Me) was prepared from 2 : 6-dihydroxy-4-methoxy-3-methylbenzophenone by the formaldehyde–sulphuric acid method in the course of 24 hours, forming yellow felted needles (0·3 g.), m. p. 202—204° (decomp.), from alcohol, readily soluble in hot acetone, and having a red-brown ferric reaction in alcohol [Found : C, 70·3; H, 5·5; OMe, 12·8. $C_{32}H_{32}O_6(OMe)_2$ requires C, 70·4; H, 5·4; OMe, 11·7%]. The *tetra-acetate* separated from ethyl acetate–light petroleum (b. p. 60—80°) in colourless needles or plates, m. p. 165—166° (Found : C, 67·2; H, 5·3. $C_{39}H_{36}O_{13}$ requires C, 67·4; H, 5·2%). Methylation of this ketone by the methyl sulphate–potassium carbonate method gave 3 : 3′-dibenzoyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexamethoxy-5 : 5′-dimethyldiphenylmethane, m. p. 168—169°, identical with an authentic specimen.

3-*Acetyl*-3′-*benzoyl*-2 : 4 : 2′ : 4′-*tetrahydroxy*-6 : 6′-*dimethoxy*-5 : 5′-*dimethyldiphenylmethane* (IX; R = Me, R′ = Ph, R″ = Me).—The mixed solid from the interaction of 2 : 6-dihydroxy-4-methoxy-3-methylbenzophenone (0·6 g.) and 2 : 6-dihydroxy-4-methoxy-3-methylacetophenone (0·5 g.) in alcohol (15 ml.), containing 40% aqueous formaldehyde (3 ml.) and concentrated sulphuric acid (1 ml.), during 24 hours was separated by crystallisation from alcohol into 3 : 3′-diacetyl-2 : 4 : 2′ : 4′-tetrahydroxy-6 : 6′-dimethoxy-5 : 5′-dimethyldiphenylmethane, m. p. 218—219° (decomp.), 3 : 3′-dibenzoyl-2 : 4 : 2′ : 4′-tetrahydroxy-6 : 6′-dimethoxy-5 : 5′-dimethyldiphenylmethane, m. p. 201—204° (decomp.), and 3-*acetyl*-3′-*benzoyl*-2 : 4 : 2′ : 4′-*tetrahydroxy*-6 : 6′-*dimethoxy*-5 : 5′-*dimethyldiphenylmethane*, forming yellow needles (0·3 g.), m. p. 195—196°, from alcohol and having a green ferric reaction (Found : C, 66·8; H, 5·8. $C_{34}H_{32}O_8$ requires C, 66·9; H, 5·6%). The *tetra-acetate* of the last compound separated from aqueous alcohol in colourless needles, m. p. 157—159° (Found : C, 64·4; H, 5·5. $C_{34}H_{34}O_{12}$ requires C, 64·3; H, 5·4%).

Disproportionation of 3-*Acetyl*-3′-*benzoyl*-2 : 4 : 2′ : 4′-*tetrahydroxy*-6 : 6′-*dimethoxy*-5 : 5′-*dimethyldiphenylmethane*.—On being boiled with acetic acid (45 ml., containing 3 ml. of water) for 15 hours this compound gave a dark yellow solid (0·7 g.) which was separated by fractional crystallisation from alcohol into 3 : 3′-diacetyl-2 : 4 : 2′ : 4′-tetrahydroxy-6 : 6′-dimethoxy-5 : 5′-dimethyldiphenylmethane, m. p. 219° (decomp.), unchanged 3-acetyl-3′-benzoyl-2 : 4 : 2′ : 4′-tetrahydroxy-6 : 6′-dimethoxy-5 : 5′-dimethyldiphenylmethane (0·22 g.), and a small amount of 3 : 3′-dibenzoyl-2 : 4 : 2′ : 4′-tetrahydroxy-6 : 6′-dimethoxy-5 : 5′-dimethyldiphenylmethane. When a mixture of 3 : 3′-diacetyl-2 : 4 : 2′ : 4′-tetrahydroxy-6 : 6′-dimethoxy-5 : 5′-dimethyldiphenylmethane (0·5 g.), 3 : 3′-dibenzoyl-2 : 4 : 2′ : 4′-tetrahydroxy-6 : 6′-dimethoxy-5 : 5′-dimethyldiphenylmethane (0·6 g.), acetic acid (45 ml.), and water (2·5 ml.) was boiled for 15 hours a mixture of the same products was obtained.

Action of C-Methylphloracetophenone on Symmetrical Diphenylmethanes.—(*a*) When a solution of 5 : 5′-diacetyl-2 : 4 : 2′ : 4′-tetrahydroxy-6 : 6′-dimethoxy-5 : 5′-dimethyldiphenylmethane (0·2 g.) and *C*-methylphloracetophenone (0·2 g.) in acetic acid (30 ml., containing 5 ml. of water) was gently heated under reflux (oil-bath at 140°), a pale yellow crystalline material began to separate and after 4 hours the mixture was cooled and filtered. Recrystallisation of this yellow solid (0·2 g.), m. p. 282—290°, from aqueous dioxan gave 5 : 5′-diacetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane in microscopic pale yellow needles, m. p. 291°. When the acetic acid filtrate was evaporated to a small volume in a vacuum and then diluted with water (20 ml.), a brown solid (0·18 g.), m. p. 184°, separated which on crystallisation from benzene (charcoal) yielded 2 : 6-dihydroxy-4-methoxy-3-methylacetophenone in pale yellow needles, m. p. 197—198°.

(*b*) When a mixture of 3 : 3′-dibenzoyl-2 : 4 : 2′ : 4′-tetrahydroxy-6 : 6′-dimethoxy-5 : 5′-dimethyldiphenylmethane (0·2 g.) and *C*-methylphloracetophenone (0·17 g.) was employed in the reaction (*a*), the product consisted of 5 : 5′-diacetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane (0·16 g.), m. p. 289—291°, and 2 : 6-dihydroxy-4-methoxy-3-methylbenzophenone (0·16 g.), m. p. 143—144°.

(*c*) Similarly, a mixture of 2 : 4 : 2′ : 4′-tetrahydroxy-6 : 6′-dimethoxy-5 : 5′-dimethyl-3 : 3′-di-β-phenylpropionyldiphenylmethane (0·2 g.) and *C*-methylphloracetophenone (0·17 g.) gave 5 : 5′-diacetyl-2 : 4 : 6 : 2′ : 4′ : 6′-hexahydroxy-3 : 3′-dimethyldiphenylmethane (III; R = Me, R′ = H) (0·16 g.), m. p. 291°, and 2 : 6-dihydroxy-4-methoxy-3-methyl-β-phenylpropiophenone (0·18 g.), m. p. 172—173°.

UNIVERSITY OF LIVERPOOL. [*Received, March 28th*, 1951.]

---

450. *The Chemistry of the Melanins. Part III.* The Synthesis of Hydroxyindoles from* p-*Benzoquinones.*

By R. J. S. BEER, KENNETH CLARKE, H. F. DAVENPORT, and ALEXANDER ROBERTSON.

Nenitzescu's method for the synthesis of hydroxyindoles has been examined and extended to the synthesis of 5-hydroxy-2 : 6-dimethyl-, 5-hydroxy-6-methoxy-2-methyl-, 5 : 6-dihydroxy-2-methyl-, and 5 : 6-dihydroxy-2 : 4 : 7-trimethyl-indole.

The following indoles have also been synthesised by the nitrostyrene method : 5-hydroxy-6-methoxy-2-methyl-, 6-hydroxy-5-methoxy-2-methyl-, 6-hydroxy-7-methoxy-, 7-hydroxy-6-methoxy-, 6-hydroxy-7-methoxy-2-methyl-, and 7-hydroxy-6-methoxy-2-methyl-indole.

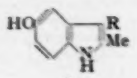
IN addition to the methods for the synthesis of hydroxyindoles described in earlier papers (*J.*, 1948, 1605, 2223; 1949, 2061) two other routes are available which differ fundamentally from the previous procedures, *viz.*, (1) the conversion of 2-(3 : 4-dihydroxyphenyl)ethylamines into 5 : 6-dihydroxyindoles by oxidation and subsequent rearrangement of the product (cf. Bu'Lock and Harley-Mason, *Nature*, 1950, **166**, 1036), and (2) the method of Nenitzescu (*Bull. Soc. Chim. Roumania*, 1929, **11**, 37) which is the subject of the present communication. This author observed that *p*-benzoquinone reacted readily with ethyl β-aminocrotonate and certain of its *N*-monosubstituted derivatives to give hydroxyindole esters to which he assigned structures of type (I) without, however, presenting evidence regarding their configurations.

From the product (I; R = CO_2Et) Nenitzescu (*loc. cit.*) obtained a poor yield of the acid (I; R = CO_2H) which on decarboxylation afforded the indole (I; R = H), the identity of which has now been confirmed by comparison with authentic 5-hydroxy-2-methylindole (*J.*, 1948, 1609). The low yield of the acid (I; R = CO_2H) has now been found to be due to decarboxylation by the hot reagent, and in this respect the hydroxyindole-3-carboxylic acids appear to be considerably less stable than the analogous 2-carboxylic acids. High yields of 5-hydroxy- and 5-methoxy-2-methylindole have been obtained by hydrolytic decomposition of the ester (I; R = CO_2Et) and its methyl ether with boiling aqueous or aqueous-alcoholic sodium hydroxide in nitrogen. By essentially the same procedure 5-hydroxy-2 : 6-dimethyl- (II; R = Me), 5-hydroxy-6-methoxy-2-methyl- (II; R = OMe), 5 : 6-dihydroxy-2-methyl- (II; R = OH) (*J.*, 1948, 2225), and 5 : 6-dihydroxy-2 : 4 : 7-trimethyl-indole (III) have been prepared respectively from methyl-, methoxy-, hydroxy-, and 2-hydroxy-3 : 6-dimethyl-*p*-

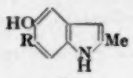
* Part II, *J.*, 1949, 2061.

benzoquinone. The orientation of (II; R = OMe) was established by its synthesis from 5-hydroxy-4-methoxy-2-nitrobenzaldehyde *via* the nitrostyrene (IV), a modification of the standard procedure being used. For comparison the isomeride, 6-hydroxy-5-methoxy-2-methylindole, was prepared from 4-hydroxy-5-methoxy-2-nitrobenzaldehyde.

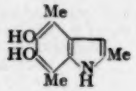
In the preparation of 5-hydroxy-4-methoxy- and 4-hydroxy-5-methoxy-2-nitrobenzaldehyde the isomerides, 3-hydroxy-4-methoxy- and 4-hydroxy-3-methoxy-2-nitrobenzaldehyde, were obtained and from these latter compounds 7-hydroxy-6-methoxy- (V) and 6-hydroxy-7-



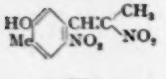
(I.)



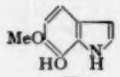
(II.)



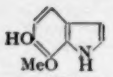
(III.)



(IV.)



(V.)



(VI.)

methoxy-indole (VI) and their 2-methyl derivatives respectively have been synthesised by the nitrostyrene method; (VI) was also prepared by the azlactone route. For the condensation of the nitroaldehydes with nitro-methane or -ethane, ammonium acetate in hot acetic acid (method of Raiford and Fox, *J. Org. Chem.*, **1944**, **9**, 170) was employed as the condensing agent in preference to alcoholic potassium hydroxide which fails in the case of 4-hydroxy-3-methoxy-2-nitrobenzaldehyde.

Experimental.

5-Hydroxy-4-methoxy-β-methyl-β : 2-dinitrostyrene.—*iso*Vanillin (Robinson and Sugasawa, *J.*, 1931, 3167) was nitrated by Pschorr's method (*Ber.*, 1902, **35**, 4396), giving 3-hydroxy- and 5-hydroxy-4-methoxy-2-nitrobenzaldehyde. The latter compound (1 g.) was heated under reflux with acetic acid (5 ml.), nitroethane (0·6 ml.), and ammonium acetate (0·4 g.) for 2 hours. On dilution with water the resulting dark brown solution deposited a dirty yellow solid which was well washed with water and crystallised from dilute alcohol, giving *5-hydroxy-4-methoxy-β-methyl-β : 2-dinitrostyrene* in brown prisms (0·8 g.), m. p. 188—189° (Found : N, 10·8. $C_{10}H_{10}O_6N_2$ requires N, 11·0%).

5-Hydroxy-6-methoxy-2-methylindole.—A mixture of the foregoing β : 2-dinitrostyrene (0·5 g.), alcohol (7 ml.), acetic acid (7 ml.), and iron powder (2 g.) was heated under reflux for 10 minutes and then filtered, and the filtrate diluted with water, neutralised with sodium hydrogen carbonate, and extracted several times with ether. Evaporation of the combined ethereal extracts left a brown gum from which *5-hydroxy-6-methoxy-2-methylindole* was isolated by extraction with boiling light petroleum (b. p. 60—80°). Crystallised from this solvent, the indole formed long, colourless needles (0·2 g.), m. p. 129°, readily soluble in the usual organic solvents except light petroleum and having a magneta Ehrlich and a red ferric reaction in alcohol (Found : C, 68·1; H, 6·6; N, 7·5. $C_{10}H_{11}O_2N$ requires C, 67·8; H, 6·2; N, 7·9%).

6-Hydroxy-5-methoxy-2-methylindole.—The condensation of 4-hydroxy-5-methoxy-2-nitrobenzaldehyde (Raiford and Stoesser, *J. Amer. Chem. Soc.*, 1928, **50**, 2559) (1 g.) with nitroethane (0·6 ml.) by the method employed for 5-hydroxy-4-methoxy-2-nitrobenzaldehyde gave rise to *4-hydroxy-5-methoxy-β-methyl-β : 2-dinitrostyrene*, which separated from alcohol and then benzene–light petroleum (b. p. 60—80°) in glistening yellow plates (0·8 g.), m. p. 97—98° (Found : N, 10·9. $C_{10}H_{10}O_6N_2$ requires N, 11·0%). Reduction of this compound (0·5 g.) with acetic acid–iron powder by the standard method gave a gum from which *6-hydroxy-5-methoxy-2-methylindole* was extracted with boiling light petroleum (b. p. 60—80°), forming colourless slender needles (0·2 g.), m. p. 136° (Found : C, 67·9; H, 6·3; N, 7·8%). This compound, which is moderately soluble in benzene or carbon tetrachloride and readily soluble in alcohol, ethyl acetate, or chloroform, gave a deep magenta Ehrlich and a red ferric reaction.

6-Hydroxy-7-methoxyindole-2-carboxylic Acid.—An intimate mixture of 4-hydroxy-3-methoxy-2-nitrobenzaldehyde (Raiford and Stoesser, *loc. cit.*) (5 g.), aceturic acid (5 g.), acetic anhydride (25 ml.), and sodium acetate (5 g.) was heated until a clear brown solution was formed. After having been kept for 10 days this mixture was treated with water (25 ml.), and the solid disintegrated, isolated, washed, and crystallised from acetic acid, giving the *4-(4-acetoxy-3-methoxy-2-nitrobenzylidene)-2-methyloxazol-5-one* in yellow prisms (4·4 g.), m. p. 215° (Found : N, 8·6. $C_{14}H_{12}O_7N_2$ requires N, 8·8%). Hydrolysis of this compound (5 g.) with dilute hydrochloric acid (50 ml.) on the steam-bath for 4½ hours afforded *4-hydroxy-3-methoxy-2-nitrophenylpyruvic acid* which, on isolation with ether, formed yellow plates (3·7 g.), m. p. 182°, from acetic acid (Found : N, 5·3. $C_{10}H_9O_7N$ requires N, 5·5%). The *oxime* separated from benzene or ethyl acetate in colourless needles, m. p. 152° (Found : N, 10·6. $C_{10}H_{10}O_7N_2$ requires N, 10·4%).

A solution of the foregoing pyruvic acid (1 g.) in alcohol (15 ml.) and acetic acid (15 ml.) containing iron powder (5 g.) was gently heated, boiled for 15 minutes, filtered, diluted with water, cooled, and extracted several times with ether. Evaporation of the dried extracts left *6-hydroxy-7-methoxyindole-2-carboxylic acid* which formed colourless needles (0·4 g.), m. p. 244—245° (decomp.), from ethyl acetate, having a green Ehrlich (with hot reagent) and a red-brown ferric reaction (Found: N, 6·8. $C_{10}H_9O_4N$ requires N, 6·8%).

6-Hydroxy-7-methoxyindole.—(*a*) 6-Hydroxy-7-methoxyindole-2-carboxylic acid (0·5 g.) was heated with glycerol (10 ml.) at 240° for 25 minutes, and the cooled solution diluted with water (50 ml.). On isolation with ether, the resulting *6-hydroxy-7-methoxyindole* formed colourless prisms (100 mg.), m. p. 85°, from light petroleum (b. p. 60—80°) (Found: C, 66·4; H, 5·8; N, 8·5. $C_9H_9O_2N$ requires C, 66·3; H, 5·5; N, 8·6%). The yield of the compound was less satisfactory when the decarboxylation was effected with copper bronze in a vacuum at 240°. This indole, which is soluble in the usual organic solvents except light petroleum, gives a pale red Ehrlich and a greenish-brown ferric reaction.

(*b*) Prepared from 4-hydroxy-3-methoxy-β : 2-dinitrostyrene (Raiford and Fox, *J. Org. Chem.*, 1944, **9**, 170) (1 g.) by the pyridine method, the acetate formed yellow plates (1·1 g.), m. p. 101—102°, from dilute alcohol. On reduction by the acetic acid–iron powder method this compound (1 g.) gave *6-acetoxy-7-methoxyindole*, which formed colourless plates (0·4 g.), m. p. 81°, from light petroleum (b. p. 60—80°) (Found: N, 7·2. $C_{11}H_{11}O_3N$ requires N, 6·8%). A solution of the acetate (0·1 g.) in methanol (3 ml.) was added to 2N-aqueous sodium hydroxide (3 ml.) containing sodium dithionite (hydrosulphite) (1 g.), and the mixture kept in a stoppered flask at 0° for 15 minutes, treated with excess of ice-cold dilute acetic acid, and extracted with ether. Evaporation of the ethereal extract gave 6-hydroxy-7-methoxyindole (70 mg.), m. p. and mixed m. p. 85—86°, after purification from light petroleum.

7-Hydroxy-6-methoxyindole.—The interaction of 3-hydroxy-4-methoxy-2-nitrobenzaldehyde (Pschorr, *loc. cit.*) (1 g.), nitromethane (0·5 ml.), and ammonium acetate (0·4 g.) in boiling acetic acid (5 ml.) for 2 hours gave *3-hydroxy-4-methoxy-β : 2-dinitrostyrene*, which separated from dilute alcohol in pale brown needles (0·8 g.), m. p. 215° (Found: N, 11·7. $C_9H_8O_6N_2$ requires N, 11·7%). Reduction of this styrene (0·5 g.) by the acetic acid–iron powder method gave rise to 7-hydroxy-6-methoxyindole, which formed colourless needles (0·14 g.), m. p. 89°, from light petroleum (b. p. 60—80°) and had a green Ehrlich (blue with warm reagent) and a brown ferric reaction (Found: C, 66·5; H, 5·7; N, 8·5. $C_9H_9O_2N$ requires C, 66·3; H, 5·5; N, 8·6%).

6-Hydroxy-7-methoxy-2-methylindole.—Prepared from 4-hydroxy-3-methoxy-2-nitrobenzaldehyde (5 g.) and nitroethane (3·2 ml.) by the ammonium acetate method, *4-hydroxy-3-methoxy-β-methyl-β : 2-dinitrostyrene* formed yellow needles (4 g.), m. p. 113—114°, from benzene (Found: N, 10·7. $C_{10}H_{10}O_6N_2$ requires N, 11·0%). By the acetic acid–iron powder reduction method this styrene (1 g.) was converted into *6-hydroxy-7-methoxy-2-methylindole*, which separated from light petroleum (b. p. 60—80°) in colourless needles (0·4 g.), m. p. 114°, moderately soluble in benzene and readily soluble in alcohol, acetone, or ethyl acetate (Found: C, 68·0; H, 6·3; N, 8·2. $C_{10}H_{11}O_2N$ requires C, 67·8; H, 6·2; N, 7·9%). This compound gives a deep magenta Ehrlich and a red alcoholic ferric reaction. Formed by the reduction of the acetate of 4-hydroxy-3-methoxy-β-methyl-β : 2-dinitrostyrene, the acetate of 6-hydroxy-7-methoxy-2-methylindole crystallised from light petroleum in colourless needles, m. p. 118—119°, and on deacetylation by the sodium hydroxide–dithionite method gave the parent indole, m. p. and mixed m. p. 114°.

7-Hydroxy-6-methoxy-2-methylindole.—By the ammonium acetate–nitroethane method 3-hydroxy-4-methoxy-2-nitrobenzaldehyde (1 g.) furnished *3-hydroxy-4-methoxy-β-methyl-β : 2-dinitrostyrene*, which crystallised from dilute alcohol in fine yellow needles (0·8 g.), m. p. 160° (Found: N, 11·4. $C_{10}H_{10}O_6N_2$ requires N, 11·0%). On reduction by the acetic acid–iron powder method during 10 minutes this compound (0·5 g.) gave *7-hydroxy-6-methoxy-2-methylindole*, forming colourless needles (100 mg.), m. p. 93°, from light petroleum (b. p. 40—60°), readily soluble in the usual organic solvents except light petroleum (Found: C, 68·1; H, 6·2; N, 8·1. $C_{10}H_{11}O_2N$ requires C, 67·8; H, 6·2; N, 7·9%). This indole gives a deep violet Ehrlich and a bright red ferric reaction.

5-Hydroxy-2-methylindole.—Hydrolysed by Nenitzescu's method (*loc. cit.*), ethyl 5-hydroxy-2-methylindole-3-carboxylate (1 g.) gave a mixture of the acid (0·2 g.), m. p. 196°, and a little 5-hydroxy-2-methylindole (0·2 g.), m. p. 134°. When the ester (1 g.) was boiled with 2N-aqueous sodium hydroxide (20 ml.) for 1 hour in nitrogen 5-hydroxy-2-methylindole was obtained in almost theoretical yield on extraction of the acidified hydrolysate with ether. Crystallised from light petroleum, it formed colourless plates (0·6 g.), identical with an authentic specimen (Beer *et al.*, *J.*, 1948, 1609). The picrate separated from benzene in red needles, m. p. 158°.

Ethyl 5-methoxy-2-methylindole-3-carboxylate (Nenitzescu, *loc. cit.*) was similarly hydrolysed with aqueous-alcoholic alkali, giving 5-methoxy-2-methylindole, m. p. 89—90°, in good yield.

Ethyl 5-Hydroxy-6-methoxy-2-methylindole-3-carboxylate.—Ethyl β-aminocrotonate (Michaelis, *Annalen*, 1909, **366**, 337) (3 g.), dissolved in the minimum amount of alcohol, was added to a solution of methoxy-*p*-benzoquinone (Erdtmann, *Proc. Roy. Soc.*, 1934, *A*, **143**, 177) (3 g.) in warm alcohol (10 ml.). The mixture was refluxed for 1 hour and then on being kept at 0° slowly deposited *ethyl 5-hydroxy-6-methoxy-2-methylindole-3-carboxylate* (2·1 g.). Crystallised from alcohol, the ester formed colourless needles, m. p. 220°, which retained solvent of crystallisation (Found, in specimen dried in a high vacuum at 80°: C, 62·4; H, 6·1; N, 5·6. $C_{13}H_{15}O_4N$ requires C, 62·7; H, 6·0; N, 5·6%).

When the condensation of the methoxy-*p*-quinone (3 g.) and ethyl β-aminocrotonate (3 g.) was effected in acetone (100 ml.) at room temperature for 24 hours the resulting ethyl 5-hydroxy-6-methoxy-2-methylindole-3-carboxylate (2 g.) was mixed with a red by-product which was removed by extraction

with boiling ligroin. Crystallised from this solvent the *substance* formed red needles, m. p. 150° (Found : C, 59·2, 59·4; H, 5·7, 5·6; N, 6·1, 6·2%).

Hydrolysis of the indole ester (1 g.) with boiling 2N-aqueous sodium hydroxide (40 ml.) in nitrogen gave 5-hydroxy-6-methoxy-2-methylindole (0·5 g.) which had m. p. and mixed m. p. 130°, after sublimation in a high vacuum followed by crystallisation from light petroleum (b. p. 80—100°). The rather unstable picrate formed red needles, m. p. 150°, from benzene.

5-Hydroxy-2 : 6-dimethylindole.—A solution of methyl-*p*-benzoquinone (Schniter, *Ber.*, 1887, **20**, 2283) and ethyl β-aminocrotonate (3 g.) in acetone (20 ml.) was boiled for 1 hour and concentrated by evaporation of part of the acetone 10 ml.) in a current of nitrogen. On being kept at 0° the residue deposited *ethyl 5-hydroxy-2 : 6-dimethylindole-3-carboxylate* (2·4 g.), which formed colourless needles, m. p. 220—221°, from alcohol (Found, in a specimen dried in a high vacuum at 80° : C, 66·8; H, 6·7; N, 6·2. $C_{13}H_{15}O_3N$ requires C, 66·9; H, 6·4; N, 6·0%). Boiled with 2N-aqueous sodium hydroxide (50 ml.) for 1 hour, this ester (1 g.) gave rise to *5-hydroxy-2 : 6-dimethylindole* (0·58 g.), which was purified by distillation in a vacuum at 130°/0·1 mm. followed by crystallisation from light petroleum (b. p. 80—100°), forming colourless plates and having an intense red Ehrlich reaction (Found : C, 74·6; H, 6·9; N, 8·5. $C_{10}H_{11}ON$ requires C, 74·5; H, 6·8; N, 8·7%). The picrate separated from benzene in red needles, m. p. 162° (decomp.).

5 : 6-Dihydroxy-2-methylindole.—The interaction of hydroxy-*p*-benzoquinone (Willstätter and Müller, *Ber.*, 1911, **44**, 2180) (3 g.) and ethyl β-aminocrotonate (3 g.) in hot alcohol (20 ml.) for 1 hour gave *ethyl 5 : 6-dihydroxy-2-methylindole-3-carboxylate*, which formed colourless needles, blackening at 200°, from alcohol (Found : C, 61·1; H, 5·6; N, 6·1. $C_{13}H_{13}O_4N$ requires C, 61·3; H, 5·5; N, 6·0%). Hydrolysis of this ester (2 g.) with boiling 2N-aqueous sodium hydroxide and distillation of the product in a high vacuum furnished 5 : 6-dihydroxy-2-methylindole, which formed colourless plates (0·3 g.), becoming black at 200° (Found : C, 66·5; H, 5·7. Calc. for $C_9H_9O_2N$: C, 66·3; H, 5·5%). Obtained in poor yield by the acetic anhydride–pyridine method, the diacetate had m. p. and mixed m. p. 134° (cf. Beer *et al.*, *loc. cit.*).

3-Hydroxy-2 : 5-dimethyl-p-benzoquinone.—A mixture of triacetoxy-*p*-xylene (Erdtmann, *loc. cit.*) (30 g.), methanol (60 ml.), and concentrated hydrochloric acid (10 ml.) was heated under reflux for 1 hour, the solvent was removed in a vacuum, and the residual pale brown solid was crystallised from ethyl acetate–light petroleum (b. p. 60—80°), giving *trihydroxy-p-xylene* in colourless needles (12 g.), m. p. 156° (Found : C, 62·3; H, 6·4. $C_8H_{10}O_3$ requires C, 62·3; H, 6·5%). This hydroxyquinol (10 g.) was oxidised with silver oxide (16 g.) in anhydrous ether (200 ml.), containing sodium sulphate (50 g.), in the course of 15 minutes and on evaporation the filtered solution left *3-hydroxy-2 : 5-dimethyl-p-benzoquinone* (8 g.), which separated from alcohol in orange plates, m. p. 135—137° (Found : C, 63·4; H, 5·5. $C_8H_8O_3$ requires C, 63·2; H, 5·3%).

5 : 6-Dihydroxy-2 : 4 : 7-trimethylindole.—Ethyl 5 : 6-dihydroxy-2 : 4 : 7-trimethylindole-3-carboxylate was prepared from 3-hydroxy-2 : 5-dimethyl-*p*-benzoquinone (1 g.) and ethyl β-aminocrotonate (1 g.) in boiling alcohol during 1 hour. On isolation the ester separated from alcohol as a *hydrate* in pale pink needles (0·85 g.), m. p. 174° (Found : C, 59·9; H, 6·9; N, 5·0. $C_{14}H_{17}O_4N,H_2O$ requires C, 59·8; H, 6·8; N, 5·0%). Hydrolysis of this compound (1 g.) followed by distillation of the product at 0·1 mm. (bath-temp. 200°) gave *5 : 6-dihydroxy-2 : 4 : 7-trimethylindole* (0·6 g.), which formed colourless plates, m. p. 168°, from benzene–light petroleum (b. p. 60—80°) (Found : C, 69·0; H, 6·9; N, 7·2. $C_{11}H_{13}O_2N$ requires C, 69·1; H, 6·8; N, 7·3%). This compound, which blackens on exposure to air, gives an intense purple Ehrlich reaction. Its solution in dilute aqueous sodium hydrogen carbonate slowly acquires a brown colour, but no melanin-like precipitate is formed.

UNIVERSITY OF LIVERPOOL.

[*Received, March 28th*, 1951.]

451. *The Kinetics of the Dehydrochlorination of Substituted Hydrocarbons. Part VII.* The Mechanism of the Thermal Decompositions of* 1 : 1 : 2 : 2- *and* 1 : 1 : 1 : 2-*Tetrachloroethane.*

By D. H. R. Barton and K. E. Howlett.

1 : 1 : 2 : 2-Tetrachloroethane decomposes in the temperature range 263—382° by a homogeneous first-order reaction to give trichloroethylene and hydrogen chloride. The rate constant equation is $k = 10^{9\cdot63}\,e^{-36,500/RT}$ sec.$^{-1}$. There is no variation in rate constant over the initial pressure range 19—83 mm. The reaction shows well-defined temperature-dependent induction periods which obey the equation $I = 10^{-15\cdot0}\,e^{44,000/RT}$ min. and are independent of the initial pressure and of the surface area : volume ratio. They can be prolonged indefinitely by the addition of propylene, the prolongation being proportional to the amount of propylene added.

1 : 1 : 1 : 2-Tetrachloroethane decomposes similarly in the temperature range 310—378° and kinetic investigations give results as above.

The decompositions of both tetrachloroethanes must be exclusively of the radical-chain type, the propagation steps involving chlorine atoms and tetrachloroethyl radicals. The chain lengths, estimated from the inhibition experiments, are about 500 at 369° for 1 : 1 : 2 : 2-tetrachloroethane and about 370 at 367° for the 1 : 1 : 1 : 2-isomer.

In previous communications the mechanisms of the thermal decompositions of ethyl chloride, 1 : 1- and 1 : 2-dichloroethane, *tert.*-butyl chloride, *iso*propyl chloride, 1 : 2-dichloropropane, and 1 : 1 : 1-trichloroethane have been elucidated (Barton and Howlett, *J.*, 1949, 155, 165; Barton and Onyon, *Trans. Faraday Soc.*, 1949, **45**, 725; *J. Amer. Chem. Soc.*, 1950, **72**, 988; Barton and Head, *Trans. Faraday Soc.*, 1950, **46**, 114). In continuation of the programme of work outlined by Barton and Onyon (*loc. cit.*), attention has been directed to the two tetrachloroethanes. According to the theoretical relation correlating mode of thermal decomposition with molecular structure (*idem*, *ibid.*), these two compounds should decompose by chain mechanisms. This inference has now been proved correct.

No previous physicochemical investigation of these decompositions has been reported.

Experimental.

Materials.—The 1 : 1 : 2 : 2- and 1 : 1 : 1 : 2-tetrachloroethanes were purified as described by Barton and Howlett (*loc. cit.*) for 1 : 2-dichloroethane, except that fractional distillation was carried out under reduced pressure. The following physical constants were recorded (the means of the best literature values are in parentheses): 1 : 1 : 2 : 2-Tetrachloroethane, b. p. 103° (corr.)/186 mm. (100°/186 mm., interpolated from Herz and Rathmann, *Chem. Zeit.*, 1912, **36**, 1417), f. p. (sulphur dioxide vapour-pressure thermometer) −44·0° (mean, −43·2°; from −43·8°, Timmermans, *Chem. Zentr.*, 1914, I, 618; −42·5°; *idem*, *Bull. Soc. chim. Belg.*, 1927, **36**, 504). 1 : 1 : 1 : 2-Tetrachloroethane, b. p. 129·5° (corr.) (129·3° from 129—129·7°, Phillips, Davies, and Mumford, *J.*, 1929, 548; 129·2°, Henne and Hubbard, *J. Amer. Chem. Soc.*, 1936, **58**, 404), f. p. (ammonia vapour-pressure thermometer, calc. from data of Stock, Henning, and Kuss, *Ber.*, 1921, **54**, 1126) −69·0° (−68·1°, Henne and Hubbard, *loc. cit.*).

Apparatus.—The apparatus and experimental technique were as used in previous work (Barton and Howlett, *loc. cit.*). In view of the low vapour pressures of the two tetrachloroethanes the dead space in the capillaries and spoon gauge was heated to about 200° by an external electrical winding. All the results recorded below were obtained in reaction vessels, the walls of which had been coated with a carbonaceous film (cf. *idem*, *loc. cit.*). The overnight pyrolysis of either of the tetrachloroethanes under the conditions mentioned below rapidly leads to the deposition of such films and there was no difficulty in repressing the heterogeneous mode of decomposition.

Results.

Stoicheiometry.—As in the earlier work of this series, the course of reaction was determined by the increase in pressure at constant volume. Figs 1 and 2, where the straight lines are drawn at the theoretical slope of 45°, refer respectively to 1 : 1 : 2 : 2- and 1 : 1 : 1 : 2-tetrachloroethane and show that the hydrogen chloride produced is equivalent to the pressure increase. The data summarised refer to

* Part VI, *J. Amer. Chem. Soc.*, 1950, **72**, 988.

various temperatures and initial pressures and were obtained from decompositions up to 75% completion. This agrees with the stoicheiometry (*A*) previously established (cf. Barton, *J.*, 1949, 148) for these reactions, but does not exclude the further possibility of reaction (*B*). That (*B*) was probably insignificant during the times required for 75% decomposition of the tetrachloroethanes was shown by a separate study with trichloroethylene. At 361°, where the half-lives of both the tetrachloroethanes were about

$$C_2H_2Cl_4 \longrightarrow CHCl{:}CCl_2 + HCl \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (A)$$
$$CHCl_2{\cdot}CCl_3 \longrightarrow CCl_2{:}CCl + HCl \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (B)$$

10 minutes, the rate of increase of pressure of trichloroethylene alone showed that its decomposition proceeded to about 10% in 3 hours. A representative hydrogen chloride titration proved that the

FIG. 1.

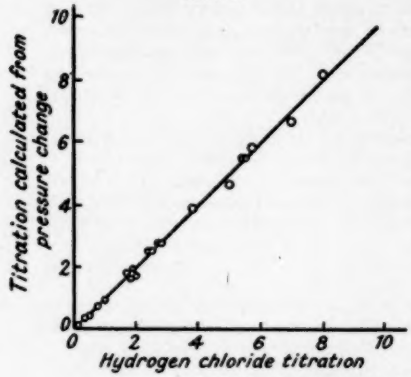
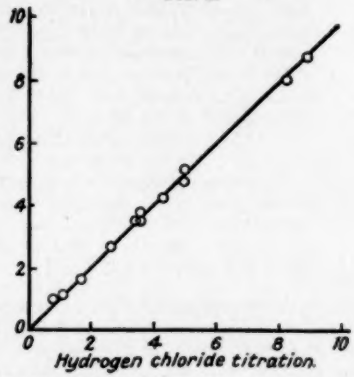


FIG. 2.



(*All titrations in terms of ml. of* 0·0189N-KOH).

FIG. 3.

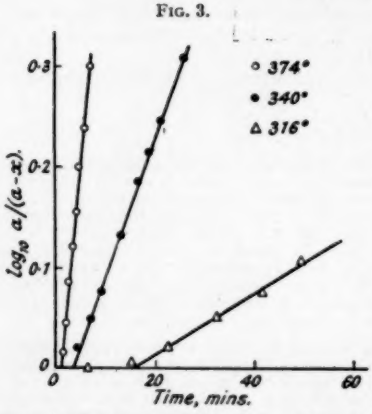
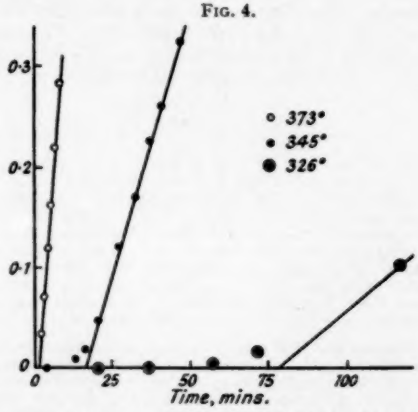


FIG. 4.



pressure increase was a real measure of the latter decomposition and that it was not invalidated by dichloroacetylene polymerisation. The results on trichloroethylene are shown in Table I.

TABLE I.

$p_0(C_2HCl_3)$, mm.	25	36	60
Time, min.	200	120	164
Δp, mm.	2·5	3	5·5*

* Titre of 0·0187N-KOH: Calc., 0·55 ml. Found, 0·55 ml.

Overnight runs with the tetrachloroethanes at the higher temperatures studied showed pressure increases of 120—130%. This is undoubtedly caused by the partial occurrence of reaction (*B*).

After about 50 experiments with each of the tetrachloroethanes a few mg. of deposit had appeared in the exit tap between the reactor and the pumping line. This was collected, dissolved in light petroleum (b. p. 40—60°), and chromatographed over alumina to remove silicone grease. The (95 : 5) light petroleum–benzene eluate furnished hexachlorobenzene which recrystallised from ethyl acetate–light petroleum as needles, m. p. 223—225° alone or mixed with an authentic specimen (m. p. 223—225°). It must be formed by the polymerisation of dichloroacetylene (Ott and Dittus, *Ber.*, 1943, **76**, 80; cf. Berthelot and Jungfleisch, *Compt. rend.*, 1869, **69**, 542; Nicodemus, *J. pr. Chem.*, 1911, [ii], **83**, 312). The isolation of hexachlorobenzene is further positive evidence for the occurrence of reaction (B).

FIG. 5.

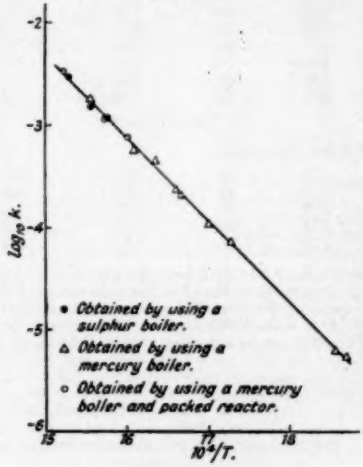


FIG. 6.

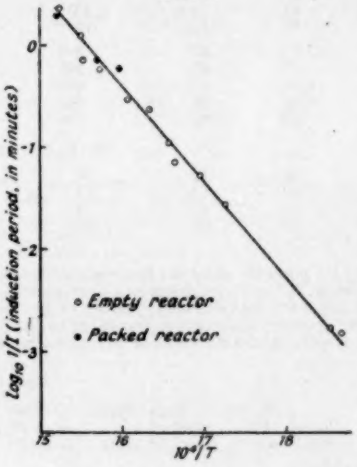


FIG. 7.

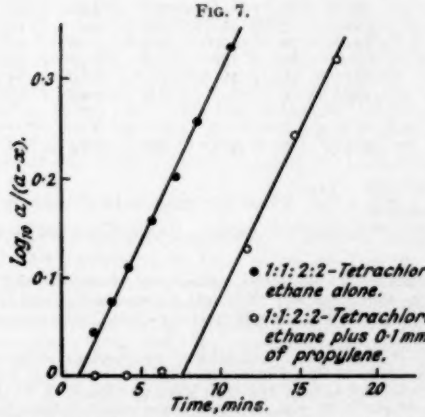
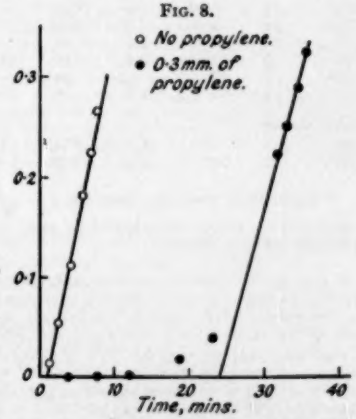


FIG. 8.



Kinetics.—With these preliminary facts established, the decompositions were studied over the temperature ranges 263—382° (for 1 : 1 : 2 : 2-) and 310—378° (for 1 : 1 : 1 : 2-tetrachloroethane). Because of the low vapour pressures of the tetrachloroethanes the results reported are not so reliable as those for 1 : 2-dichloroethane (Barton and Howlett, *loc. cit.*). A fairly comprehensive study has been made of the 1 : 1 : 2 : 2-tetrachloroethane decomposition but only a cursory investigation is reported for the 1 : 1 : 1 : 2-isomer. Nevertheless, as will be seen later, there can be no doubt as to the mechanisms involved.

At all temperatures the reactions followed first-order kinetics up to at least 60% decomposition. Some typical runs are illustrated in Fig. 3 for the symmetrical, and in Fig. 4 for the unsymmetrical, compound. As with 1 : 2-dichloroethane (*idem*, *loc. cit.*) and 1 : 1 : 1-trichloroethane (Barton and Onyon, *loc. cit.*), the reactions showed well-defined temperature-dependent induction periods of moderate

reproducibility. These are also illustrated in Figs. 3 and 4. As shown by the data in Table II, there was no variation in first-order velocity constant over the pressure ranges 19—83 mm. and 31—85 mm. for the 1 : 1 : 2 : 2- and the 1 : 1 : 1 : 2-compound, respectively.

TABLE II.

Temp.	p_0 ($C_2H_2Cl_4$), mm.	10^5k, sec.$^{-1}$.	Induction period (I), min.	Temp.	p_0 ($C_2H_2Cl_4$), mm.	10^5k, sec.$^{-1}$.	Induction period (I), min.
			(*a*) 1 : 1 : 2 : 2-*Tetrachloroethane.*				
316°	27	12·0	9	362°	22	114	0·8
316	64	11·9	15	362	29	128	0·8
316	70	12·0	17	362	36	118	1·5
339	19	46	3·0	362	40	121	1·1
339	27	45	3·5	362 [a]	47	131	0·9
339	38	47	5·7	362	51	121	1·2
339	44	50	3·7	362 [a]	83	116	1·5
339	56	42	5·0				

[a] Packed reactor.

			(*b*) 1 : 1 : 1 : 2-*Tetrachloroethane.*				
345	32	45	16	373	31	155	1·1
345	58	45	11	373	43	167	1·9
345	72	45	5	373	55	154	1·5
345	85	42	17	373	62	171	1·3
				373	75	152	1·4

Table III gives the observed first-order rate constants for 1 : 1 : 2 : 2-tetrachloroethane. A graph of $\log_{10}k$ against $1/T$ gave a satisfactory straight line, as illustrated in Fig. 5. The rate constant equation for 1 : 1 : 2 : 2-tetrachloroethane, calculated by the least-squares method, the same statistical weight being given to every observation, was found to be $k = 10^{9\cdot62}\,e^{-36,500/RT}$ sec.$^{-1}$. As usual with the chain-type decompositions in our series of investigations, we prefer not to attach error limits to this expression.

TABLE III.

Temp.	No. of runs.	Mean 10^5k, sec.$^{-1}$.	% Mean error of mean k.[a]	Mean I, min.	% Mean error of mean I.[a]	Temp.	No. of runs.	Mean 10^5k, sec.$^{-1}$.	% Mean error of mean k.[a]	Mean I, min.	% Mean error of mean I.[a]
Empty reactor.											
263°	1	0·56	—	724	—	339°	14	47	4·2	4·0	36
266	1	0·65	—	600	—	349	2	57	5·2	3·5	20
306	2	7·3	2·7	34	6	362 [b]	28	120	3·3	1·99	17
316	5	11·6	3·5	16	14	370 [b]	10	156	3·2	1·29	13
328	1	22	—	14	—	371	11	187	2·7	0·79	14
330	4	24	1·7	9	16	380 [b]	9	307	2·0	0·43	32
Packed reactor.											
352	7	77	3·2	1·70	11	382	6	343	2·3	0·62	15
362·5	6	119	5·9	1·35	8						

[a] Calculated from the formula $\sigma = \sqrt{\frac{\Sigma(x-\bar{x})^2}{n(n-1)}} \times \frac{100}{\bar{x}}$, where the symbols have their usual significance. [b] Results obtained by using sulphur as thermostatic vapour. In all other experiments mercury was employed.

A number of experiments were made in a packed reactor where the surface area : volume ratio had been increased by a factor of about 4 over that in the empty reactor. The data, summarised in Table III and illustrated in Fig. 5, show that the rate of decomposition was unaffected by packing. The reaction must, therefore, be homogeneous (see also below).

The induction periods for 1 : 1 : 2 : 2-tetrachloroethane were substantially independent of initial pressure; if anything there was a tendency for them to be longer at higher pressures (see Table II*a*). A graph of $\log_{10}$ of the mean induction periods (Table III) against $1/T$ gave a straight line (Fig. 6), the equation of which may be expressed as $I = 10^{-15\cdot0}\,e^{44,000/RT}$ min., where I is the observed induction period. Table III and Fig. 6 also show that packing did not alter the length of the induction periods.

For the 1 : 1 : 1 : 2-tetrachloroethane decomposition the mean rate constant (from 7 runs) at 353·5° was $60 \pm 3 \times 10^{-5}$ sec.$^{-1}$. In the packed reactor (approximately 4-fold increase in surface area : volume ratio) at 354° the result (6 runs) was $72 \pm 1 \times 10^{-5}$ sec.$^{-1}$. This reaction is therefore also homogeneous. The induction periods seemed to be independent of initial pressure and of packing.

One of the most interesting features of the 1 : 1 : 2 : 2-tetrachloroethane pyrolysis was the effect of adding propylene. Previously, we have shown that this hydrocarbon is a powerful inhibitor for the chain-type decompositions of 1 : 2-dichloroethane and of 1 : 1 : 1-trichloroethane, the rate constant being thereby reduced to a limiting figure independent of further propylene addition. With 1 : 1 : 2 : 2-tetrachloroethane, propylene caused a lengthening of the induction period already present. Throughout most of the prolonged induction period the reaction velocity appeared to be zero, and at the end, the

rate of decomposition rose again quite rapidly to the normal value. Fig. 7 illustrates some typical results from experiments carried out at 370°. It was confirmed by hydrogen chloride titrations that little, if any, decomposition occurred during these propylene-induced induction periods. The increase in the length of the induction period (for a standard initial pressure of 1 : 1 : 2 : 2-tetrachloroethane) was approximately proportional to the amount of propylene added. The data in Table IV, obtained at 369°, illustrate this point.

TABLE IV.

$p_0(C_2H_2Cl_4)$, mm.	$p(C_2H_4)$, mm.	I, min.	$p(C_2H_4)$ corr. to $p_0(C_2H_2Cl_4)$ = 50 mm.	ΔI/corr. $p(C_2H_4)$.	$p_0(C_2H_2Cl_4)$, mm.	$p(C_2H_4)$, mm.	I, min.	$p(C_2H_4)$ corr. to $p_0(C_2H_2Cl_4)$ = 50 mm.	ΔI/corr. $p(C_2H_4)$.
1 : 1 : 2 : 2-*Tetrachloroethane.*					1 : 1 : 1 : 2-*Tetrachloroethane.*				
—	0	1·2	0	—	—	0	1·5	—	—
42	0·03	5	0·036	106	41	0·12	12	0·15	70
41	0·05	7	0·061	95	58	0·3	25	0·26	90
58	0·10	9	0·086	91	89	0·3	22	0·17	121
45	0·20	25	0·22	107	53	0·5	50	0·47	103
33	0·60	75	0·91	81	50	1·0	90	1·0	89

The effect of propylene on the 1 : 1 : 1 : 2-tetrachloroethane decomposition (at 367°) was similar, the addition prolonging the already present induction period (Fig. 8). The increase in the length of the induction period (for a standard initial pressure) was again approximately proportional to the amount of propylene added. Table IV, showing results at 367°, illustrates this. Titrations of hydrogen chloride confirmed that there was no significant decomposition during the artificially prolonged induction periods.

When the rate of a homogeneous chemical reaction is retarded by relatively small additions of a molecular species not normally participating in the reaction and, after a time, the rate of reaction increases again to the normal value, at least two interpretations can be put forward. The first, and seemingly more probable view (see Staveley and Hinshelwood, *Proc. Roy. Soc.*, 1937, *A*, **159**, 192) holds that the inhibitor is completely consumed during the initial period. Echols and Pease (*J. Amer. Chem. Soc.*, 1937, **59**, 766; 1938, **60**, 1701; 1939, **61**, 1024), however, during a study of the inhibition of butane pyrolysis by nitric oxide, obtained evidence that the inhibitor was not wholly removed during this time. They suggested that the transient retardation was due to the setting up of an equilibrium between nitric oxide, the various radicals in the system, and the " nitric oxide complexes " formed therefrom. When sufficient of these complexes had been produced it was thought that there was a " feed back " of radicals, so that reaction proceeded again at the normal rate. Propylene was found to behave similarly although the evidence was somewhat less conclusive.

To distinguish between these possibilities in our case, 0·5 mm. of propylene was added to 50 mm. of 1 : 1 : 2 : 2-tetrachloroethane at 367°. When the induction period was over and the rate had just reached normal (about 1 hour), the contents of the reactor were condensed out in a liquid-nitrogen trap. Only about 15% of the 1 : 1 : 2 : 2-tetrachloroethane had by that time decomposed, so that if an equilibrium had been set up, an appreciable quantity of propylene should have remained. The liquid-nitrogen trap was allowed to warm up and the first 8 mm. of gaseous products were returned to the reactor. Since any " propylene complexes " are presumably less volatile than propylene itself, the returned gas should have been enriched in this olefin. However, admixture with a further 50 mm. of 1 : 1 : 2 : 2-tetrachloroethane gave only the normal induction period and rate. Such experiments indicate that the propylene is completely consumed during the induction period.

DISCUSSION.

The existence of temperature-dependent induction periods, and especially the remarkable inhibition produced by very small amounts of propylene, is a proof that the thermal decompositions of 1 : 1 : 2 : 2- and 1 : 1 : 1 : 2-tetrachloroethane proceed by a homogeneous radical-chain mechanism. The fact that, in each case, the addition of propylene causes a directly proportional increase in the length of the induction period (and that no decomposition occurs during this time) means that the reactions must proceed entirely by this chain mechanism. As far as we are aware, this is the first occasion on which such a phenomenon has been noted in the pyrolysis of organic compounds (compare Goldfinger, *Faraday Soc. Discussion*, 1947, **2**, 149).

Our interpretation of the more intimate aspects of the 1 : 1 : 2 : 2-tetrachloroethane pyrolysis follows closely upon our similar treatment of the 1 : 2-dichloroethane decomposition. The reaction mechanism may be represented by the following four steps.

Initiation. (i) Kinetically first-order decomposition of the 1 : 1 : 2 : 2-tetrachloroethane to furnish, either directly or indirectly, chlorine atoms.

Propagation. (ii) $Cl + CHCl_2{\cdot}CHCl_2 \longrightarrow HCl + {\cdot}CCl_2{\cdot}CHCl_2$.

(iii) ${\cdot}CCl_2{\cdot}CHCl_2 \longrightarrow CCl_2{:}CHCl + Cl$.

Termination. (iv) $Cl + {\cdot}CCl_2{\cdot}CHCl_2 \longrightarrow HCl + CCl_2{:}CCl_2$.

Steps (ii) and (iii) explain the stoicheiometry of the reaction, steps (i) and (iv) the first-order kinetics.

By assuming in the propylene inhibition experiments that one molecule of propylene prevents the occurrence of one kinetic chain, it is possible to compute the chain length of the 1 : 1 : 2 : 2-tetrachloroethane decomposition. Thus we have :

Chain length = Rate of overall reaction/Rate of initiating reaction. At 369° the initial overall rate of decomposition of 50 mm. of the reactant is 5·2 mm. min.$^{-1}$. At this temperature the rate of consumption of propylene (= rate of initiating step) was (see p. 2037) 1/96 mm. min.$^{-1}$. Hence the chain length is 5·2 × 96 (= about 500).

The more detailed mechanism of the 1 : 1 : 1 : 2-tetrachloroethane decomposition may be represented similarly. A calculation of the chain length at 367°, similar to that made for the symmetrical isomer, indicates a value of 3·9 × 95 (= about 370).

So far in this series of papers we have not discussed the origin of the naturally occurring induction periods found with chlorinated hydrocarbons which decompose by the radical-chain mechanism. Two reasonable explanations may be advanced : (*a*) that the induction period represents the time required to destroy inhibitors, and (*b*) that it represents the time required to build up the steady-state concentration of the chain-carrying species. It should be possible to distinguish between these alternatives by admitting reactant to the reactor, pumping it out again into a cold trap at the end of the induction period, and then readmitting it. If (*a*) is correct then on readmission of the reactant there should be no further induction period, while if (*b*) is correct the induction period should be unchanged no matter how many times this experiment is repeated. The vapour pressures of the tetrachloroethanes are inconveniently low for this test to be applied, but experiments on 1 : 1 : 1-trichloroethane (Onyon, Ph.D.Thesis, London, 1950) show that (*b*) is correct for this compound, and similar results have been obtained with 1 : 2-dichloroethane (Barton and Head, unpublished). It is very probable that the same explanation holds for the two tetrachloroethanes, especially as we believe that we have been working with pure specimens of these compounds.

The fact that the induction periods are unaltered on packing the reactor is of importance for a finer aspect of the mechanism of the decomposition of the two tetrachloroethanes and also of 1 : 2-dichloroethane. A radical-chain reaction of this type, if initiated *and terminated* on the reactor walls, might well appear homogeneous when the reactor is packed. However, if the induction periods arise in the way we believe, and they are unchanged, as we have observed, on packing the reactor, then the chains cannot be initiated at the walls. Thus these decompositions are truly homogeneous radical-chain reactions. The chain-carrying species responsible for the induction periods would seem to be the " large " chlorinated alkyl radical, *e.g.*, $\cdot CHCl\cdot CH_2Cl$ in the case of 1 : 2-dichloroethane.

A more quantitative treatment of the induction periods found with 1 : 2-dichloroethane and other aspects of mechanism will be discussed by one of us (K. E. H.) in a later paper.

We thank the Central Research Fund of London University for a grant in aid of this investigation.

Birkbeck College Research Laboratory,
21 Torrington Sq., London, W.C.1.
Bedford College, Regent's Park, London, N.W.1. [*Received, February 27th*, 1951.]

452. *The Kinetics of the Dehydrochlorination of Substituted Hydrocarbons. Part VIII.* The Mechanisms of the Thermal Decompositions of* n-*Propyl and* n-*Butyl Chloride and 2 : 2′-Dichlorodiethyl Ether.*

By D. H. R. Barton, A. J. Head, and R. J. Williams.

n-Propyl chloride decomposes in the temperature range 693—751° K. by a homogeneous, first-order reaction to give, stoicheiometrically, propylene and hydrogen chloride. *n*-Butyl chloride decomposes in the temperature range 700—744° K. by a similar homogeneous, first-order reaction to furnish butene and hydrogen chloride; neither with the former over the pressure range 50—155 mm., nor with the latter over the range 10—135 mm., is there any falling off in rate constant with lowering of initial pressure. The rate constant equation for propyl chloride is given by $k = 10^{13\cdot45 \pm 0\cdot35}e^{(-55{,}000 \pm 1{,}200)/RT}$ sec.$^{-1}$, and that for butyl chloride by $k = 10^{14\cdot0 \pm 0\cdot1}e^{(-57{,}000 \pm 400)/RT}$ sec.$^{-1}$. Neither decomposition is subject to the slightest inhibition on addition of propylene, and neither gives any indication of temperature-dependent induction periods. The reactions are regarded as unambiguous examples of unimolecular decompositions.

2 : 2′-Dichlorodiethyl ether decomposes in the temperature range 646—702° K. by a first-order reaction. The reaction products are a complex mixture. The rate-constant equation can be approximately represented by $k = 10^{14}e^{-54{,}500/RT}$ sec.$^{-1}$ at 30 mm. initial pressure. The rate constant fell over the pressure range 65·8—16·7 mm. In all experiments moderately reproducible induction periods were observed. These were inversely dependent on the temperature and on the initial pressure. They could be prolonged indefinitely by the addition of propylene, the increase in the length of the induction period being proportional to the amount of propylene added. The rate of decomposition was reduced by packing the reactor, the induction periods being thereby lengthened. The decomposition of 2 : 2′-dichlorodiethyl ether must be exclusively of the radical-chain type. The termination step proceeds, at least in part, on the walls of the reactor. The chain length, estimated from inhibition experiments in the packed reactor, was about 23 at 686° K. for 30 mm. initial pressure of reactant.

This paper reports a continuation of our studies on the thermal decomposition of saturated chlorinated hydrocarbons. Previously we had suggested (Barton and Onyon, *Trans. Faraday Soc.*, 1949, **45**, 725) that *n*-propyl and *n*-butyl chloride would decompose by homogeneous first-order reactions, the mechanisms of which would be unimolecular. This suggestion was based on the fact that propylene (and doubtless also butene) is a powerful inhibitor for the chain type of decomposition shown by 1 : 2-dichloroethane (Barton and Howlett, *J.*, 1949, 155), 1 : 1 : 1-trichloroethane (Barton and Onyon, *J. Amer. Chem. Soc.*, 1950, **72**, 988), and the two tetrachloroethanes (Barton and Howlett, preceding paper), and therefore, if it were a reaction product, it could not be produced by a chain mechanism. The decomposition would thus proceed by an alternative mechanism which, if homogeneous, would be of the unimolecular type (compare Barton and Onyon, *loc. cit.*, 1949). This view now receives confirmation.

We have also investigated the thermal decomposition of 2 : 2′-dichlorodiethyl ether. Here it was not possible to make a firm prediction as to the mode of decomposition because if the attack of chloride atoms were preferentially at a 2-(C–H) bond, as in (*A*), then a reaction chain could not be propagated, whereas if the attack were at a 1-(C–H) bond, as in (*B*), then chain propagation (cf. Ash and H. C. Brown, *Records of Chemical Progress*, 1948, p. 81) would be facilitated. As shown below, the chlorinated ether actually decomposes by the chain mechanism, although the reaction is a complex one and not suited for detailed quantitative study.

(*A*) $Cl + Cl{\cdot}C_2H_4{\cdot}O{\cdot}CH_2{\cdot}CH_2Cl \longrightarrow HCl + Cl{\cdot}C_2H_4{\cdot}O{\cdot}CH_2{\cdot}\dot{C}HCl$

$Cl{\cdot}C_2H_4{\cdot}O{\cdot}CH_2{\cdot}\dot{C}HCl \longrightarrow$ (no ready loss of a chlorine atom)

(*B*) $Cl + Cl{\cdot}C_2H_4{\cdot}O{\cdot}CH_2{\cdot}CH_2Cl \longrightarrow HCl + Cl{\cdot}C_2H_4{\cdot}O{\cdot}\dot{C}H{\cdot}CH_2Cl$

$Cl{\cdot}C_2H_4{\cdot}O{\cdot}\dot{C}H{\cdot}CH_2Cl \longrightarrow Cl{\cdot}C_2H_4{\cdot}O{\cdot}CH{:}CH_2 + Cl$ (ready loss of β-chlorine atom)

No physicochemical investigation of these decompositions has hitherto been reported.

* Part VII, preceding paper.

Experimental.

Materials.—Difficulty was found in the purification of *n*-propyl chloride. The commercial material, purified by the general method described by Barton and Howlett (*J.*, 1949, 155) and crystallised twice, gave kinetic runs characterised by a fast start. When the partly decomposed propyl chloride was frozen out of the reactor, and the undecomposed propyl chloride vapour then re-admitted, the fast start was no longer apparent and the kinetics were of first order from zero time. This behaviour indicated that a readily decomposed contaminant had resisted the purification procedure. The impure propyl chloride was then refluxed with concentrated sulphuric acid for 30 minutes and worked up again by the usual procedure. Two low-temperature crystallisations afforded material which showed no fast start and gave satisfactory first-order kinetics (see p. 2042). The following constants were recorded for the purified material and are compared with the means of the best literature values (in parentheses): b. p. 46·9° (corr.)/760 mm. (mean 46·6°, corr.: from 46·8°, Berthoud, *J. Chim. physique*, 1917, **15**, 3; 46·6°, Timmermans and Hennault-Roland, *ibid.*, 1930, **27**, 401; 46·5°, Mumford and Phillips, *J.*, 1950, 75); $d_4^{21\cdot1}$ 0·8900 (mean 0·8900: interpolated from d_4^{15} 0·8985, d_4^{20} 0·8799, Timmermans and Hennault-Roland, *loc. cit.*; d_4^{20} 0·8890, d_4^{25} 0·8830, Mumford and Phillips, *loc. cit.*); $n_D^{23\cdot6}$ 1·3863 (cf. n_D^{20} 1·3900, Mumford and Phillips, *loc. cit.*).

Difficulty was also experienced in the purification of *n*-butyl chloride. Treatment of the commercial material in the usual way (Barton and Howlett, *loc. cit.*), including two low-temperature crystallisations, gave material which also exhibited fast starts. Further purification, involving refluxing with concentrated sulphuric acid for 35 minutes, furnished a preparation of b. p. 77·8—78·4°/760 mm. The last and main fraction, b. p. 78·4° (corr.)/760 mm., gave satisfactory first-order kinetics. It was further fractionated by one low-temperature crystallisation without alteration of the kinetic behaviour. The following constants were recorded for the purified material and are compared with the means of the best literature values (in parentheses): b. p. 78·4°/760 mm. (mean 78·4° corr.: from 78·6°, Timmermans, *Bull. Soc. chim. Belg.*, 1921, **30**, 65; 78·5°, Timmermans and Hennault-Roland, *loc. cit.*; 78·5°, Smyth and McAlpine, *J. Chem. Physics*, 1935, **3**, 347; 77·9°, Vogel, *J.*, 1943, 636; 78·4°, Mumford and Phillips, *loc. cit.*); $d_4^{23\cdot5}$ 0·8829 (mean 0·8827; interpolated from d_4^{15} 0·89197, d_4^{30} 0·87549, Timmermans and Hennault-Roland, *loc. cit.*; d_4^{20} 0·8866, Vogel, *loc. cit.*; d_4^{20} 0·8866, and d_4^{25} 0·8811, Mumford and Phillips, *loc. cit.*); n_D^{23} 1·4010 (compare n_D^{20} 1·4023, Smyth and McAlpine, *loc. cit.*; n_D^{20} 1·4023, Wiswall and Smyth, *J. Chem. Physics*, 1941, **9**, 356; n_D^{20} 1·4022, Vogel, *loc. cit.*; n_D^{20} 1·4021, Mumford and Phillips, *loc. cit.*).

Commercial 2 : 2′-dichlorodiethyl ether was washed several times with concentrated hydrochloric acid and then fractionally distilled under reduced pressure. The following constants were recorded for the purified material and are compared with the means of the best literature values (in parentheses): b. p. 178·7—178·9° (corr.)/760 mm. (mean 178·4°: from 178·75°, Gallaugher and Hibbert, *J. Amer. Chem. Soc.*, 1937, **59**, 2521; 178·6°, Tschamler, *Monatsh.*, 1948, **78**, 297; 177·9°, Mumford and Phillips, *loc. cit.*); d_4^{26} 1·2121 (1·2118: extrapolated from d_4^{20} 1·2192, d_4^{25} 1·2130, Mumford and Phillips, *loc. cit.*); n_D^{20} 1·4568 (mean 1·4572: from n_D^{20} 1·4570, Gallaugher and Hibbert, *J. Amer. Chem. Soc.*, 1936, **58**, 813; n_D^{20} 1·4573, Mumford and Phillips, *loc. cit.*; n_D^{20} 1·4574, Tschamler, *loc. cit.*).

Apparatus.—The apparatus and experimental technique were those detailed by Barton and Howlett (*J.*, 1949, 155). Because of the low vapour pressure of 2 : 2′-dichlorodiethyl ether the same precautions with regard to the heating of the dead space were adopted as for the two tetrachloroethanes (see preceding paper). All the results recorded below were obtained in reaction vessels the walls of which had been coated with a carbonaceous film (cf. Barton and Howlett, *loc. cit.*; Barton and Onyon, *Trans. Faraday Soc.*, 1949, **45**, 725). The kinetics of the reactions were elucidated by following the increase in pressure at constant volume as in all the previous papers of this series.

Results.

Stoicheiometry.—By analogy with work in previous Parts of this series (see especially Barton, *J.*, 1949, 148; Barton and Onyon, *Trans. Faraday Soc.*, 1949, **45**, 725; Barton and Head, *ibid.*, 1950, **46**, 114) it was expected that *n*-propyl and *n*-butyl chloride would decompose according to (*C*) and (*D*) respectively. This was confirmed by the fact that the final pressure in the reactor after a long run was

$$(C)\quad CH_3{\cdot}CH_2{\cdot}CH_2Cl \longrightarrow CH_3{\cdot}CH{:}CH_2 + HCl$$
$$(D)\quad CH_3{\cdot}[CH_2]_2{\cdot}CH_2Cl \longrightarrow CH_3{\cdot}CH_2{\cdot}CH{:}CH_2 + HCl$$

close to twice the initial pressure (Table I). However for butyl chloride the ratio increased above the theoretical value in the higher part of the temperature range investigated.

The decomposition of 2 : 2′-dichlorodiethyl ether furnished a mixture of products. We assume that

$$(E)\quad (CH_2Cl{\cdot}CH_2)_2O \longrightarrow (CH_2{:}CH)_2O + 2HCl$$

the stoicheiometry of the initially occurring reaction is represented by (*E*), and that this is followed by the (slower) decomposition of divinyl ether, a reaction known to furnish a complicated mixture of products (H. A. Taylor *J. Chem. Physics*, 1936, **4**, 116). In agreement, the ratio of the final to the initial pressure, p_f/p_0, for long-term experiments (Table I) exceeded 4·0, and the ratio p/p_0 at times equal to several half-lives of the decomposing dichloro-ether approached 3·0, the final approach to 4·0 and higher ratios being much slower. It is of interest to compare these values of p_f/p_0 with those obtained by Taylor (*loc. cit.*) for divinyl ether at 723—773° K. Taylor's data being accepted, a value of 4·05—4·24 can be computed for the decomposition of 2 : 2′-dichlorodiethyl ether in this temperature range. In presenting the results for this ether the stoicheiometry (*E*) has been assumed throughout.

Kinetics.—All three decompositions exhibited first-order kinetics as illustrated by Fig. 1 (*n*-propyl chloride), Fig. 2 (*n*-butyl chloride), and Fig. 3 (2 : 2′-dichlorodiethyl ether). In all experiments with the monochloro-compounds there were no indications of induction periods even at the lowest temperatures studied (compare Figs. 1 and 2). In contrast, the decomposition of 2 : 2′-dichlorodiethyl ether (see Fig. 3) exhibited temperature-dependent induction periods. The variation of velocity constant with initial pressure was insignificant over the pressure range 50—155 mm. for *n*-propyl chloride and 10—135 mm. for *n*-butyl chloride (Table II). With the dichloro-ether, both the rate constants and the

TABLE I.

Temp., °K.	p_0, mm.	Time of reaction, hrs.	p_t/p_0.	Temp., °K.	p_0, mm.	Time of reaction, hrs.	p_t/p_0.	Temp., °K.	p_0, mm.	Time of reaction, hrs.	p_t/p_0.
***n*-Propyl chloride.**											
Unpacked reactor.											
693	128·4	19	1·96	729	109·7	18	2·03	744	107·9	18	2·03
695	123·3	70	1·95	729	88·3	20	2·06	745	97·1	19	2·08
705	93·3	18	1·98			44	2·09	746	48·7	18	2·10
713	88·1	70	2·04	734	68·2	18	2·09	746	50·3	18	2·08
716	110·2	18	2·03	734	97	18	2·02	746	51·7	19	2·06
724	47·7	18	2·06	734	104·2	18	2·03	746	80·6	18	2·06
724	103·1	18	1·97	739	91·8	19	2·03	746	80·8	18	2·07
728	43·3	19	2·06	739	102·1	18	2·06				
Packed reactor.											
719	103·5	18	1·98	732	103·6	18	2·04	738	100·7	18	2·01
719	95·8	18	1·98	735	101·1	18	2·04	740	91·6	22	2·08
732	64·1	22	2·12	735	105·9	18	2·00	740	105·8	18	2·02
732	82·9	21	2·07	738	98·4	19	2·06	741	110·1	19	2·05
***n*-Butyl chloride.**											
Unpacked reactor.											
700	102·1	16	2·01	723	74·5	16	2·14	730	70·3	16	2·18
700	113·9	16	2·03	723	69·0	16	2·10	738	68·2	16	2·24
700	90·2	39	2·08	723	76·9	16	2·14	744	66·2	16	2·35
712	116·2	17	2·08	723	75·0	46	2·30	744	63·7	19	2·36
712	89·2	16	2·08	730	91·0	18	2·20	744	55·6	68	2·56
716	107·5	17	2·09								
Packed reactor.											
712	71·5	42	2·19	729	60·2	20	2·18	729	70·6	16	2·24
712	63·5	16	2·08	729	71·0	16	2·22	729	74·0	16	2·24
729	61·0	16	2·18								
2 : 2′-Dichlorodiethyl ether.											
Unpacked reactor.											
647	30·2	16	3·55	684	31·5	16	4·10	684	27·9	16	4·06
671	29·6	46	4·21	684	29·0	66	4·38	684	33·0	16	4·06
673	26·2	16	4·01								
Packed reactor.											
683	30·7	16	4·14	683	30·4	46	4·19	689	30·0	16	4·00
683	30·5	16	4·08	689	31·1	16	4·11				

TABLE II.

p_0, mm.	10^4k, sec.$^{-1}$.	p_0, mm.	10^4k, sec.$^{-1}$.	p_0, mm.	10^4k, sec.$^{-1}$.	p_0, mm.	10^4k, sec.$^{-1}$.
***n*-Propyl chloride at** 736° K. (unpacked reactor).							
53·2	9·04	98·4	8·93	105·6	8·92	132·1	9·02
69·9	8·92	100·2	9·10	111·2	8·94	154·4	8·83
91·2	8·82	103·1	8·95				
***n*-Butyl chloride at** 737·6° K. (unpacked reactor).							
31·1	14·0	70·1	13·7	94·8	13·7	134·6	13·4
46·4	12·9	80·3	13·0	110·2	13·8		
***n*-Butyl chloride at** 712·1° K. (packed reactor).							
10·4	3·27	17·5	3·39	29·4	3·48	52·4	3·46
16·7	3·68	19·4	3·43	40·6	3·42	*ca.* 70	3·39

FIG. 1.

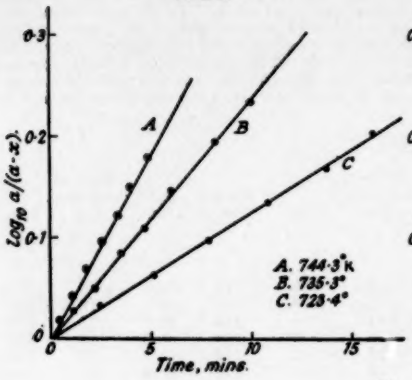


FIG. 2.

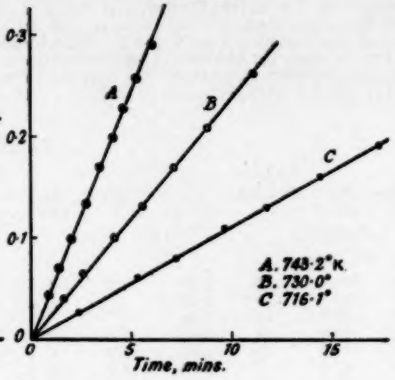


FIG. 3.

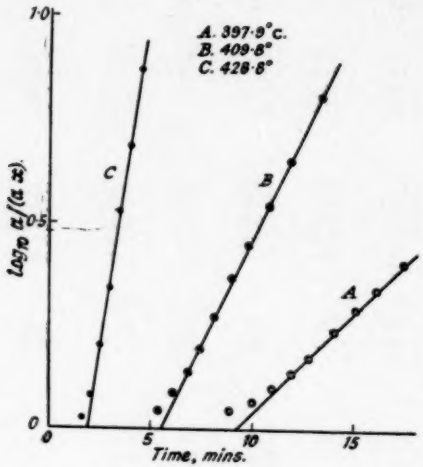
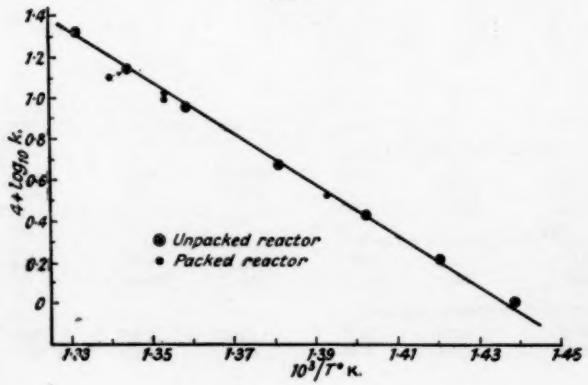


FIG. 4.



induction periods varied with the initial pressure of reactant over the range 16·7—65·8 mm. (Table III). It was of interest that the induction periods observed were inversely proportional to the initial pressures (Table III).

TABLE III.

p_0, mm.	16·7	23·5	32·2	65·8
10^4k, sec.$^{-1}$ *	9·3	17·5	25·9	30·4
Induction period, I, min.	16·0	10·6	7·7	3·3
$p_0 \times I \times 10^{-2}$, mm. min.	2·67	2·49	2·48	2·17

* Packed reactor at 685·5° K.

The rate-constant equations over the pressure ranges studied (see above) were given by $k = 10^{13\cdot45 \pm 0\cdot35}e^{(-55{,}500 \pm 1200)/RT}$ sec.$^{-1}$ for *n*-propyl chloride and by $k = 10^{14\cdot0 \pm 0\cdot1}e^{(-57{,}000 \pm 400)/RT}$ sec.$^{-1}$ for *n*-butyl chloride. The rate data are summarised in Table IV and illustrated further in Fig. 4 (*n*-propyl chloride) and Fig. 5 (*n*-butyl chloride). The straight lines in these figures have been drawn by the least-squares method, the same statistical weight being given to every observation of k. The error limits have been computed by the procedure detailed by Barton and Onyon (*loc. cit.*, 1949). Packing the reactor (see Table IV and Figs. 4 and 5) with glass tubing to give an approximately 6-fold increase in the surface area : volume ratio had a negligible effect on the rates of decomposition of *n*-propyl and *n*-butyl chloride and therefore the reactions must be homogeneous.

TABLE IV.

Temp., °K.	No. of runs.	Mean $k \times 10^4$, sec.$^{-1}$.	% Standard deviation of mean k.*	Temp., °K.	No. of runs.	Mean $k \times 10^4$, sec.$^{-1}$.	% Standard deviation of mean k.*
n-Propyl chloride.							
Unpacked reactor.							
695·0	7	1·02	0·6	736·0	10	8·95	0·3
704·0	6	1·65	0·4	744·0	19	13·85	0·4
713·0	5	2·68	0·5	751·0	7	21·0	0·9
724·0	7	4·76	0·6				
Packed reactor.							
718·0	7	3·34	0·8	744·0	12	13·88	0·5
739·0	29	9·89	0·4				
n-Butyl chloride.							
Unpacked reactor.							
700·0	23	1·70	0·4	723·0	25	6·26	0·4
708·7	7	2·72	0·7	730·2	11	9·09	0·5
712·4	13	3·42	0·7	737·6	9	13·52	0·7
715·7	10	4·09	0·7	743·6	18	18·75	0·5
Packed reactor.							
712·1	11	3·58	0·5	729·2	18	8·75	0·4

* Given by $100 \times \sqrt{\frac{\Sigma(x - \bar{x})^2}{n(n-1)}} \Big/ \bar{x}$, where the symbols have the usual significance.

The rate-constant equation for 2 : 2′-dichlorodiethyl ether at initial pressures close to 30 mm. was given by $k = 10^{15}e^{-54{,}500/RT}$ sec.$^{-1}$ (experiments in the unpacked reactor). The rate-constant data, together with the appropriate induction periods, which decreased with increasing temperature, are summarised in Table V. We do not attach a high degree of accuracy to the data. Packing the reactor as for *n*-propyl and *n*-butyl chloride (see above) caused an approximate halving of the rate of decomposition and an approximate doubling of the induction periods (see Table V).

TABLE V.

Temp., °K.	No. of runs.	Mean 10^4k, sec.$^{-1}$.	% Standard deviation of mean k.*	Mean I, min.	Based on no. of runs.	% Standard deviation of mean I.*
Unpacked reactor.						
646·2	4	4·19	1·6	36·4	2	—
671·1	11	20·1	2·0	9·1	8	2·9
683·6	11	40·8	1·1	5·5	9	5·9
702·0	10	123·0	1·2	1·7	9	2·5
Packed reactor.						
686·2	36	21·0	1·5	9·0	30	2·0

* Calculated as in Table IV.

FIG. 5.

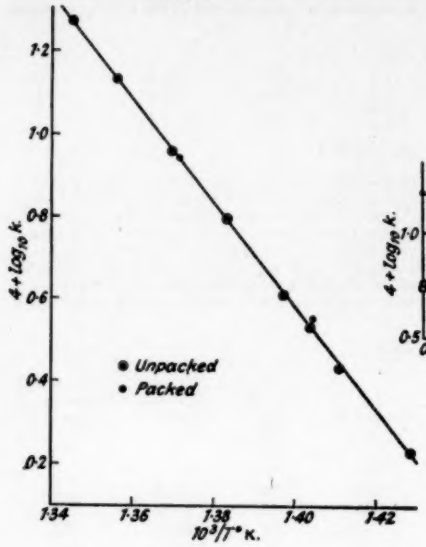


FIG. 6.

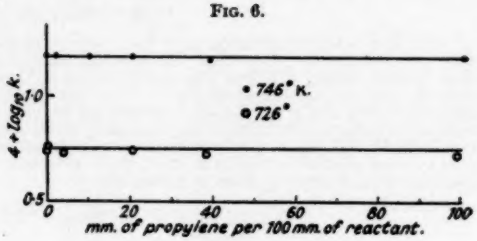


FIG. 7.

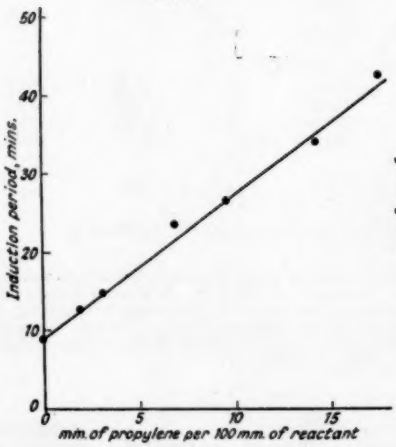
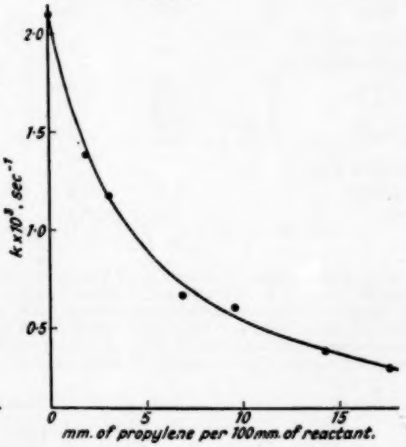


FIG. 8.



The addition of propylene to decomposing *n*-propyl and *n*-butyl chloride had no effect. This is illustrated by Fig. 6 for *n*-propyl chloride (initial pressures close to 50 mm.) and by Table VI for *n*-butyl chloride. In all cases the kinetics remained of the first order.

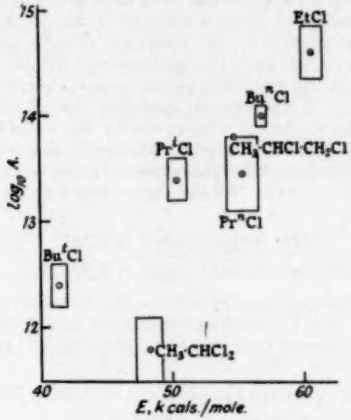
TABLE VI.

n-Butyl chloride, mm.	10—135	107·6	112·8	105·9	104·2
Propylene, mm.	0	0·4	0·8	1·5	3·7
10^4k, sec.$^{-1}$ *	3·40	3·55	3·51	3·39	3·42

* All experiments at 712·4° K. in the unpacked reactor.

The effect of adding propylene to decomposing 2 : 2′-dichlorodiethyl ether was quite different. First, the already present induction periods were prolonged in proportion to the amount of propylene added, as shown in Fig. 7, which refers to runs in the packed reactor at 686·2° K. with initial pressures close to 30 mm. Secondly, whilst the reaction continued to exhibit first-order kinetics, the rate of decomposition of the 2 : 2′-dichlorodiethyl ether, after the induction period was over, was reduced, the reduction in rate increasing with the concentration of added propylene. Fig. 8, which refers to experiments under the same conditions as for Fig. 7, is illustrative.

FIG. 9.



DISCUSSION.

The thermal decompositions of *n*-propyl and *n*-butyl chloride follow first-order kinetics, the rate constants *not* varying with the initial pressure. The reactions are homogeneous, exhibit no induction periods even at the lowest temperatures studied, and are totally unaffected by the addition of propylene. All these experimental features are identical with those established previously for ethyl chloride, 1 : 1-dichloroethane, *tert.*-butyl chloride, *iso*propyl chloride, and 1 : 2-dichloropropane (Barton and Howlett, *J.*, 1949, 165; Barton and Onyon, *Trans. Faraday Soc.*, 1949, **45**, 725; Barton and Head, *ibid.*, 1950, **46**, 114), and, without repeating the arguments in detail, we regard them as adequate to prove that *n*-propyl and *n*-butyl chloride decompose by the unimolecular mechanism.

In a previous paper (Barton and Head, *loc. cit.*) it was shown that there was a linear relationship between $\log_{10}$ of the non-exponential terms of the rate-constant equations and the corresponding activation energies for the decompositions of ethyl chloride, *iso*propyl chloride, and *tert.*-butyl chloride, reactions which are authenticated as unimolecular. It is of interest that the data for *n*-propyl and *n*-butyl chloride (see Fig. 9) also fall on the same straight line within the error limits indicated by the rectangles. The data for 1 : 2-dichloropropane are also included, but without error limits. The data for 1 : 1-dichloroethane, however, do not fall on the line.

Although also exhibiting first-order kinetics, the decomposition of 2 : 2′-dichlorodiethyl ether shows temperature-dependent induction periods which are prolonged proportionately by the addition of small amounts of propylene. The rate of decomposition after the induction period is also reduced by addition of propylene. The reaction is *slower* in the packed than in the empty reactor, and the induction periods are longer. In contrast to the unimolecular type of decomposition (see above), the rate constant varies with the initial pressure. We regard these experimental facts as proof that decomposition of the dichloro-ether proceeds by the radical-chain mechanism (see Barton and Howlett, *J.*, 1949, 155), and further that the prolongation of the natural induction periods shows the decomposition to be 100% of the chain type (compare Barton and Howlett, preceding paper). Following the argument in the preceding paper, it is possible to calculate the kinetic chain length from the inhibition studies summarised in the Experimental Section as about 23 (packed reactor, 686·2° K., $p_0 \sim 30$ mm.). The reduction in rate constant on packing the reactor and on reducing the initial pressure of reactant implies that, as with the

decomposition of 1 : 1 : 1-trichloroethane (Barton and Onyon, *loc. cit.*, 1950), the reaction chains are, at least in part, terminated at the reactor walls.

The experimental results do not furnish a complete picture of the more intimate aspects of the 2 : 2′-dichlorodiethyl ether decomposition. However, the validity of first-order kinetics suggests that the second elimination of hydrogen chloride is much more rapid than the first. The nature of the first propagation step has already been discussed (p. 2039).

Ash and H. C. Brown's important paper (*loc. cit.*) makes it desirable to discuss in somewhat greater detail the relation between molecular structure and mode of thermal decomposition which we have previously established (Barton and Onyon, *loc. cit.*, 1949). Ash and Brown have pointed out that, if allowance is made for the formation of C_2H_4 by β-elimination of a chlorine atom from the $\cdot CH_2 \cdot CH_2Cl$ radical, then the predominant attack of chlorine atoms on ethyl chloride is at the β- and not at the α-position (as one would conclude from the ratio of 1 : 1- to 1 : 2-dichloroethanes formed). If this view be accepted, then it remains to explain why ethyl chloride and 1 : 1-dichloroethane should decompose by the unimolecular rather than by the radical-chain mechanism. Now, if a saturated chlorinated hydrocarbon is pyrolysed to eliminate hydrogen chloride,* the mechanism, if homogeneous, may be unimolecular or of radical-chain character (Barton and Onyon, *loc. cit.*). We can regard the two mechanisms as competitive, the relative rates being given by

$$\text{Rate (unimolecular)} = k_1[A] \qquad \text{(i)}$$

$$\text{and Rate (radical chain)} = k_2[Cl][A] \qquad \text{(ii)}$$

where [A] represents the concentration of chlorinated hydrocarbon and the other symbols have the usual significance. For 1 : 2-dichloroethane and the more highly chlorinated ethanes a β-chlorine atom can be eliminated from the 1 : 2-dichloroethyl radical intermediate and thus continue the chain :

$$Cl + CH_2Cl \cdot CH_2Cl \longrightarrow HCl + \cdot CHCl \cdot CH_2Cl$$

$$\cdot CHCl \cdot CH_2Cl \longrightarrow CHCl{:}CH_2 + Cl$$

This is also the case for β-attack on ethyl chloride and 1 : 1-dichloroethane, but α-attack on these compounds gives rise to " dead " radicals which cannot propagate the chain by β-elimination and thus act as chain terminators :

$$Cl + CH_3 \cdot CH_2Cl \longrightarrow HCl + CH_3 \cdot \dot{C}HCl \text{ (no β-elimination)}$$

$$Cl + CH_3 \cdot CHCl_2 \longrightarrow HCl + CH_3 \cdot \dot{C}Cl_2 \text{ (no β-elimination)}$$

The chain length of the radical decomposition of ethyl chloride is thus limited to the ratio of β- to α-attack in the chlorination reaction. Such a value (about 10) is negligible compared with the probable chain length (about 10^4) of the radical-chain decomposition of (say) 1 : 2-dichloroethane. The unimolecular mode of decomposition is thus greatly favoured. The same argument applies for the case of 1 : 1-dichloroethane.

Further illustrations of the relationship between molecular structure and mode of thermal decomposition will be given in later papers.

We thank the Central Research Fund of London University for a Grant in aid of this investigation, which was carried out during the tenure of a Postgraduate Studentship in the University (A. J. H.). We also thank the D.S.I.R. for a Maintenance Grant (R. J. W.).

Birkbeck College Research Laboratory,
21, Torrington Sq., London, W.C.1.
Imperial College of Science and Technology,
S. Kensington, London, S.W.7.

[*Received, February 27th*, 1951.]

* We assume that the necessary stereochemical requirements for the unimolecular elimination are satisfied (Barton, *J.*, 1949, 2174; Barton and Head, *Trans. Faraday Soc.*, 1950, **46**, 114; Barton, Head, and Williams, forthcoming paper).

453. *Magnetochemistry of the Heaviest Elements. Part IV.* Plutonium Trifluoride and Trichloride.*

By J. K. Dawson, C. J. Mandleberg, and D. Davies.

The magnetic susceptibilities of plutonium trifluoride and trichloride have been measured over the temperature range 90—600° K. There is a minimum between 500° and 550° K. in the susceptibility–temperature curve of the tervalent plutonium ion, and the close resemblance of this behaviour to that of the tervalent samarium ion is taken as good qualitative evidence for a $5f^5$ electronic configuration for the plutonium ion. The application of Van Vleck's method for calculating the theoretical susceptibility yields 58 as the most probable value of the spin-doublet screening constant.

In the rare-earth series, the magnetic susceptibility of the tervalent samarium ion varies with temperature in an unusual way. Hund assumed the multiplet intervals to be large compared to kT, and calculated the magnetic susceptibilities of the rare-earth ions on this basis: his results agreed well with experiment except for samarium and europium. Van Vleck ("The Theory of Electric and Magnetic Susceptibilities," O.U.P., 1932, Chap. IX) has shown that the discrepancy can be removed satisfactorily by taking into account the possibility that in samarium and europium the multiplet intervals may be comparable with kT; the Boltzmann temperature factor enters into the calculation, and the contribution to the susceptibility of the term arising from the second-order Zeeman effect cannot then be neglected. Such an assumption accounts for the fact that the susceptibility of Sm(III) does not obey the Weiss–Curie law, and in particular that it exhibits a shallow minimum somewhat above room temperature, the exact position of which on the theoretical curves depends upon the value of the screening constant used in the calculations.

With the same number of unpaired f electrons postulated for both samarium and plutonium (Seaborg, "The Transuranium Elements," National Nuclear Energy Series, 14B, paper 21.1), their tervalent compounds might be expected to behave similarly, but no magnetic measurements have hitherto been reported on plutonium compounds over a sufficiently wide temperature range to confirm this. Howland and Calvin (U.S. Atomic Energy Commission Report, A.E.C.D. 2440) find that Pu(III) in dilute hydrochloric acid solution has a susceptibility of 370×10^{-6}, and Elliott and Lewis (American Chemical Society meeting, Chicago, September 1950) report that plutonium trifluoride has susceptibilities of 2550, 1590, and 1150×10^{-6}, at 76°, 189·5°, and 303° K., respectively (claiming that the results follow the Weiss–Curie law with $\mu = 1{\cdot}96$, $\Delta = 110°$), and that the oxalate, $Pu_2(C_2O_4)_3.9H_2O$, gives the values 1580, 850, and 620×10^{-6} at 76°, 190°, and 298° K. In the present investigation, the authors report measurements made on the Pu(III) ion in the solid fluoride and chloride over the temperature range 90—600° K.

Experimental.

The measurements were made on a balance described previously (Dawson and Lister, *J.*, 1950, 2177). The samples (1—10 mg.) were sealed in small Pyrex or quartz capillaries, and after the measurements these were broken open, the samples washed out, and the halves of each capillary fused together again so that the effect of the empty container could be measured. Corrections were applied for the diamagnetism of the various ions (see Angus, *Proc. Roy. Soc.*, 1932, *A*, **136**, 569). The values used were: $Pu(III) = 35 \times 10^{-6}$, $Cl^- = 23 \times 10^{-6}$, and $F^- = 7{\cdot}3 \times 10^{-6}$.

Preparation of Plutonium Fluoride.—Plutonium tetraoxalate was precipitated from a pure solution of the tetranitrate by addition of oxalic acid. The centrifuged oxalate was dried by infra-red heating and transferred to a small platinum boat. A "reactive" oxide was produced by calcining it at about 600° C. in a slow stream of air, and this oxide was then allowed to react in a copper furnace at 650° C. with hydrogen fluoride containing a small partial pressure of hydrogen. The identity of the product as plutonium trifluoride was established by its X-ray diffraction pattern and by oxidation of a weighed amount to PuO_2; the change in weight corresponded to a fluorine content of 19·4 ± 0·2% (Calc.: 19·26%).

Preparation of Plutonium Chloride.—The reactive oxide was produced in the same way as in the preparation of the fluoride and it was then transferred to a quartz capillary tube which could be attached to a high-vacuum line. Carbon tetrachloride was used as the chlorinating agent (for details see Abraham *et al.*, National Nuclear Energy Series, 14B, p. 746).

The chloride sublimed out of the reaction zone and condensed in a cool section of the capillary where it was sealed off in a length of tube suitable for the magnetic measurements. After these had

* Part III, *J.*, 1951, 429.

been made, the weighed product was dissolved in dilute nitric acid and made up to a known volume in a standard flask. The solution was quite clear and had the characteristic colour of the Pu(III) ion; aliquots of this solution were evaporated to dryness and estimation by α-counting gave a plutonium content of 68·9 ± 1% (Calc.: 69·2%).

TABLE I.

Magnetic susceptibilities of PuF_3 *and* $PuCl_3$.

	PuF_3,	χPu(III)		$PuCl_3$,	χPu(III)		$PuCl_3$,	χPu(III)
T, °K.	χ g. × 10^6.	× 10^6.	T, °K.	χ g. × 10^6.	× 10^6.	T, °K.	χ g. × 10^6.	× 10^6.
90	7·38	2240	90	4·35	1607	457	1·19	515
200	3·23	1014	200	2·27	887	491	1·10	484
300	2·00	651	300	1·60	658	520	1·04	464
372	1·53	508	334	1·45	606	548	1·03	462
453	1·15	398	373	1·35	571	583	1·06	472
511	0·995	351	397	1·29	548	300	1·60	659
563	1·08	375	428	1·22	525			
594	1·14	394						
300	2·00	650						

The analyses of the compounds were not in themselves sufficiently accurate to preclude the possibility of the presence of ferromagnetic impurity sufficient to make an appreciable contribution to the susceptibilities, but samples prepared from batches of plutonium nitrate solution which had been through several different purification procedures showed good agreement amongst themselves. Results from typical runs are set out in Table I. In order to check that decomposition of the samples did not take place at the highest temperature, the room-temperature reading was repeated at the end of each run.

DISCUSSION.

If there is an actinide ion with a low-lying energy term $^6H_{5/2}$ and an electron configuration $5f^5$, analogous to the corresponding $4f^5$ state of Sm(III), then a similar deviation of the susceptibility from the Weiss–Curie law should exist. In this case there should be an appreciable contribution from the second-order Zeeman effect due to the multiplet intervals being comparable to kT, and it is therefore necessary to use Van Vleck's general formula to calculate the theoretical susceptibility :

$$\chi = \frac{N \sum_{J=L-S}^{L+S} [g_J^2 \cdot \beta^2 \cdot J(J+1)/3kT + \alpha_J](2J+1) \cdot e^{-W_J^\circ/kT}}{(2J+1) \cdot e^{-W_J^\circ/kT}}$$

where

N = Avogadro's number

$$g_J = [1 + J(J+1) + S(S+1) - L(L+1)]/2J(J+1)$$

$$\beta = eh/4\pi mc = 0{\cdot}9174 \times 10^{-20} \text{ erg gauss}^{-1}$$

$$\alpha_J = \frac{\beta^2}{6(2J+1)}\left[\frac{F(J+1)}{h\nu(J+1;\ J)} - \frac{F(J)}{h\nu(J;\ J-1)}\right]$$

$$F(J) = 1/J[(S+L+1)^2 - J^2][J^2 - (S-L)^2]$$

$$W_J^\circ = W_J - W_{J\,\text{min.}}$$

$$\frac{1}{C}\Delta\nu J_{\text{max.}} - J_{\text{min.}} = \pm \frac{5{\cdot}82(2L+1)}{n^3 l(l+1)(2l+1)} \cdot (Z - \sigma_2)^4 \text{ cm.}^{-1}$$

σ_2 = the spin-doublet screening constant

The multiplet width $\Delta\nu$, and consequently the susceptibility derived from it, are obviously very dependent on the effect of the screening of the electrons concerned by the other electrons in the ion, as expressed by the term $(Z - \sigma_2)^4$.

A $5f^5$ electron configuration with Russell–Saunders coupling being assumed, values for the ionic susceptibility were calculated for various values of σ_2 over the temperature range 50—700° K., and the results are given in Table II.

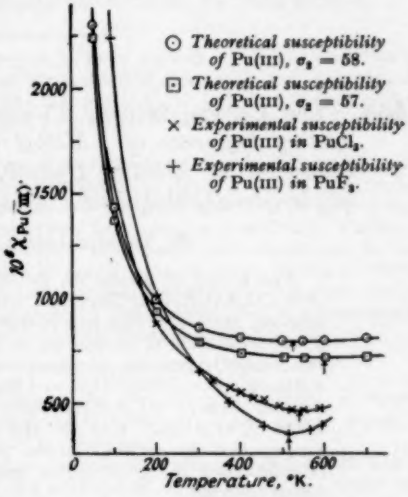
TABLE II.

Theoretical susceptibilities ($\chi \times 10^6$) *for an ion with* $5f^5$ *electron configuration.*

Screening constant σ_2 =	54.	57.	58.	59.	Screening constant σ_2 =	54.	57.	58.	59.
Temp., ° K.					Temp., ° K.				
50	2114	2249	2306	2373	500	551	718	796	892
100	1241	1375	1433	1500	550	540	714	796	895
200	804	939	997	1065	600	533	714	799	900
300	659	797	860	935	700	524	718	806	911
400	588	739	810	896					

The results for $\sigma_2 = 57$ and $\sigma_2 = 58$ are plotted in the figure, together with the experimental results on the Pu(III) ion from Table I. The theoretical curves for $\sigma_2 = 57$, 58, and 59 have shallow susceptibility minima at about 600, 530, and 480° K., respectively, whereas the experimental curves show considerably more marked minima at about 515° and 545° K. for the trifluoride and the trichloride, respectively.

The theoretical spin-only value of the magnetic moment is 5·92 Bohr magnetons, while the values obtained by Hund's method are 0·84 with Russell–Saunders coupling and 2·54 with *jj* coupling, these being independent of temperature. At room temperature the experimental moment of Pu(III) calculated from the susceptibilities by means of the formula $\mu = 2{\cdot}83\sqrt{\chi . T}$ is 1·26 in the chloride and 1·25 in the fluoride. If there is any orbital quenching due to the 5*f* electrons being less effectively sequestered than 4*f* electrons, then the moment should be higher than 0·84, becoming progressively closer to 5·92 as the quenching becomes more complete. In solution, where ionic interactions should have the least effect, Calvin, Kasha, and Sheline (National Nuclear Energy Series, 14B, paper 4.23) have found that the effective moment of Pu(III) is 1·1 Bohr magnetons. These figures may all be correlated by assuming that the Pu(III) ion has a $5f^5$ electron configuration; the "ideal" magnetic moment is 0·84, being increased to 1·1 in solution and somewhat higher in the solid compounds where the orbital interactions are greater. However, the Hund theory does not allow for any change of the moment with temperature, and in particular does not explain the susceptibility minimum above room temperature. Satisfactory correlation of theory with experiment cannot be obtained on the basis of *jj* coupling or by assuming a $5f^4 . 6d^1$ electron configuration. The Van Vleck method of calculation gives moments which are not far removed from the experimental ones, the agreement being nearest below room temperature. Table III gives the moments calculated from the susceptibilities of Table II and interpolated susceptibilities from the figure.



The similarity of the ranges of values, together with the fact that the Van Vleck calculation for a $5f^5$ configuration provides an explanation of the susceptibility minimum, may be taken as good qualitative evidence that the electronic structure of Pu(III) involves the $5f^5$ state, being closely analogous to the $4f^5$ state in Sm(III). The theoretical curve which shows a minimum susceptibility in the same temperature range as the experimental curves is the one derived by taking 58 as the value of the spin-doublet screening constant. The susceptibilities obtained by using a screening constant of 54 are in better agreement with the experimental values above room temperature but do not show a minimum in the temperature range under investigation.

If it is assumed that the theoretical curve with $\sigma_2 = 58$ is the most probable one, there remains the discrepancy that at the higher temperatures the experimental magnetic susceptibilities are lower than the theoretical ones, whereas any mechanism leading to slight orbital quenching would be expected to raise the susceptibility (towards the spin-only value). However, comparison between the molar susceptibilities of the aqueous cations of the actinide elements and those of the rare earths shows that throughout the series from one to six unpaired electrons

TABLE III.

The magnetic moment of Pu(III).

T, °K.	100	200	300	400	500
μ, $\sigma_2 = 58$	1·07	1·26	1·44	1·63	1·79
μ, PuF_3	1·25	1·28	1·25	1·22	1·20
μ, $PuCl_3$	1·08	1·19	1·26	1·32	1·38

those of the former are all appreciably lower than those of the latter (Howland and Calvin, *loc. cit.*).

Finally, it may be noted that the above results, where they are in the same temperature range, are in reasonable agreement with those of Elliott and Lewis on the hydrated Pu(III) oxalate but not at all with their results on plutonium trifluoride. In addition, it has been shown above that their contention that the susceptibility of plutonium trifluoride follows the Weiss–Curie law arises from the limited temperature range over which their results are quoted.

This paper was submitted in manuscript to Professor E. C. Stoner and the authors would like to express their thanks to him for his interest and for his helpful comments; however, the opinions expressed herein remain the sole responsibility of the authors.

The authors thank the Director of the Atomic Energy Research Establishment for permission to publish this paper.

A.E.R.E., HARWELL, NEAR DIDCOT, BERKS. [*Received, March 19th*, 1951.]

---

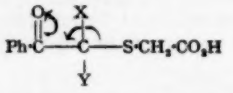
454. *The Carbon–Sulphur Fission in Thio-ethers. Part I. The Retarding Influence of α-Methyl Groups and of the Length of the Acid Chain on the Alkaline Hydrolysis of* (2-*Ketoalkylthio*)- *and* (p-*Nitrotriphenylmethylthio*)-*acetic Acids.*

By YOUSSEF ISKANDER and RASMY TEWFIK.

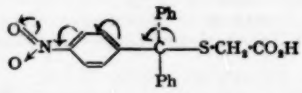
The action of alkalis on thio-ethers of the structure Ph·CO·CXY·SZ (Z = CH_2·CO_2H, CH_2·CH_2·CO_2H, CHMe·CO_2H, or CMe_2·CO_2H) was found to take any of the following four courses: (*a*) a C–SZ fission, (*b*) a CO–C fission, (*c*) a combination of (*a*) and (*b*), or (*d*) no fission whatever. The fission (*a*) was gradually retarded by introduction of one or two methyl groups in the α-position (Z = CHMe·CO_2H or CMe_2·CO_2H) or by increase in the length of the acid chain (Z = CH_2·CH_2·CO_2H). Where X = Y = Ph, and less readily where X = H and Y = Ph, the retardation of the C–SZ fission was accompanied by a CO–C fission, but where X = Y = H and where the retardation of the C–SZ fission was complete (Z = CMe_2·CO_2H) no CO–C fission occurred.

In the compounds *p*-NO_2·C_6H_4·CPh_2·SZ it was also found that when Z = CHMe·CO_2H the C–SZ fission was slower than when Z = CH_2·CO_2H and was completely absent when Z = CH_2·CH_2·CO_2H or CMe_2·CO_2H. The significance of these results is discussed.

THE alkaline hydrolysis of thio-ethers of the general formula R·SZ was discussed by Iskander (*J.*, 1948, 1549) and shown to depend on the electron deficiency at the sulphur atom caused by electron-attractive groups in R such as the carbonyl or the nitro-group in the β- or a β-conjugated position:



and



The attachment of phenyl groups to the α-position in R caused retardation of the hydrolysis with a consequent attack of the alkali on the carbonyl group, while in Z the length of the chain of the acid was found also to be a retarding factor. In order to clarify these views, experiments were designed to amplify the last two factors and to introduce a third one, namely, the attachment of methyl groups at the α-position in Z. The following table combines

the results now described with some previously recorded (standard time of the hydrolysis experiments was 30 minutes except as otherwise stated) :

R.	(1) SZ = S·CH_2·CO_2H.	(2) SZ = S·CHMe·CO_2H.	(3) SZ = S·CMe_2·CO_2H.	(4) SZ = S·CH_2·CH_2·CO_2H.
Ph·CO·CH_2	CO–C–$^{\downarrow}$S[1]	CO–C–$^{\downarrow}$S	CO–C–$^{\downarrow}$S trace	CO–C–$^{\downarrow}$S 40%
Ph·CO·CHPh	CO–C–$^{\downarrow}$S[1] 3·5 min.[a]	CO$^{\downarrow}$–C–$^{\downarrow}$S 20% 80%	CO$^{\downarrow}$–C–S	CO–C–$^{\downarrow}$S[1] 15% (20 min.)
Ph·CO·CPh_2	CO$^{\downarrow}$–C–$^{\downarrow}$S[1] 20% 80%	CO$^{\downarrow}$–C–S	CO$^{\downarrow}$–C–S	CO$^{\downarrow}$–C–S[1]
NO_2·C_6H_4·CPh_2	C–$^{\downarrow}$S[1] 5 min.	C–$^{\downarrow}$S 15 min.	unchanged	unchanged

[1] Holmberg, *Chem. Zentr.*, 1936, I, 4564. [2] Behaghel and Schneider, *Ber.*, 1935, **68**, 1588.
[3] Schönberg and Iskander, *J.*, 1942, 90.

It is seen that all the α-thio-*iso*butyric acids (col. 3) have resisted hydrolysis completely except for a trace in the phenacyl compound, and the α-thio-propionic acids (col. 2) occupied intermediate position between these acids and the thio-acetic acids (col. 1). Similarly, the β-thio-propionic acids (col. 4) occupy an intermediate position between the α-thio-propionic acids and *iso*butyric acids.

In the phenacyl series of compounds, where no phenyl groups hinder the C–S fission, one methyl group attached to the α-position in Z was not sufficient to retard the hydrolysis, while two methyl groups could stop it completely; on the other hand, increase in the length of the acid chain could lead to a C–S fission only of 40% after ½ hour's boiling with alkali. Furthermore, in all the compounds of this series no elimination of the benzoyl group occurs even in the case of α-(phenacylthio)*iso*butyric acid where the C–S fission was completely hindered, while in the cases of α-(α-benzoylbenzylthio)- and α-(benzoydiphenylmethylthio)-*iso*butyric acids complete elimination of the benzoyl group readily occurs. This is clearly due to the increased possibility in the phenacyl compounds for enol formation by the action of the alkali :

$$Ph{\cdot}CO{\cdot}CH_2{\cdot}S{\cdot}CMe_2{\cdot}CO_2H + 2NaOH \longrightarrow Ph{\cdot}C(ONa){:}CH{\cdot}S{\cdot}CMe_2{\cdot}CO_2Na + 2H_2O$$

and accordingly no seat for the nucleophilic reagent will be available (cf. Beckham, *J. Amer. Chem. Soc.*, 1934, **56**, 1122, who found that cleavage of diketones of the general formula R·CO·CHR'·COR'' occurs on the unenolised side of the diketone).

It appears from the above results that the factors decreasing the strengths of the acids under discussion, *i.e.*, the length of the acid chain or the substitution of the α-hydrogen atoms by methyl groups, were the same factors that retarded the C–S fission of these thio-ethers, enriching the sulphur atom with electrons in the same way as they must have transmitted a $+I$ effect towards the carboxyl group :

and accordingly the alkali attacks and eliminates the carbonyl group in the α-benzoylbenzyl and the α-benzoyldiphenylmethyl compounds, or forms the enolate compound with the phenacyl compounds, while the *p*-nitrotriphenylmethylthio-acids containing these retarding factors are recovered unchanged.

Experimental.

Microanalyses are by Drs. Weiler and Strauss, Oxford. M. p.s are uncorrected.

α-(*Phenacylthio*)*propionic Acid*.—Phenacyl chloride (3·1 g.) in alcohol (40 c.c.) was treated with a solution of α-mercaptopropionic acid (2·1 g.) and sodium hydrogen carbonate (4·3 g.) in water (20 c.c.), and the mixture boiled on the water-bath for 15 minutes. (Continued boiling caused gradual formation and deepening of a yellow colour.) Cooling, dilution with water, extraction with ether to remove any turbidity, and finally acidification gave the *acid* (4·1 g.) which separated from carbon tetrachloride in prisms, m. p. 90—92° (Found : C, 58·6; H, 5·5; S, 14·1. $C_{11}H_{12}O_3S$ requires C, 58·9; H, 5·4; S, 14·3%).

Alkaline hydrolysis. The acid (4 g.) in 5% sodium hydroxide solution (100 c.c.) was boiled for 0·5 hour, the colour of the solution changing from yellow through orange to light red, while oily drops collected on the surface of the solution. The oil, extracted with ether, proved to be acetophenone (1·6 g.), and the alkaline solution on acidification gave only hydrogen sulphide and colloidal sulphur.

β-(Phenacylthio)propionic Acid.—Prepared from phenacyl chloride (3·1 g.) and β-mercaptopropionic acid (2·1 g.) and isolated by the method described above, the *acid* (4·2 g.) crystallised from dilute alcohol in colourless needles, m. p. 63—65° (Found : C, 54·5; H, 6·1; S, 13·5. $C_{11}H_{12}O_3S,H_2O$ requires C, 54·5; H, 5·8; S, 13·2%).

Alkaline hydrolysis. The acid (2 g.) was hydrolysed as above. The oil (few drops), extracted with ether, was identified as acetophenone, and the yellow alkaline solution, on acidification, gave hydrogen sulphide and a yellow precipitate (1·2 g.) which separated from dilute alcohol as yellow crystals, m. p. 63—65° alone or mixed with the original acid. Repeated crystallisation from carbon tetrachloride gave the colourless form of the acid.

α-(Phenacylthio)isobutyric Acid.—Prepared from phenacyl chloride (3·1 g.) and α-mercapto*iso*butyric acid (2·4 g.) as above, the *acid* (4·6 g.) separated from carbon tetrachloride in fine needles, m. p. 107—108° (Found : C, 60·5; H, 5·9; S, 13·3. $C_{12}H_{14}O_3S$ requires C, 60·5; H, 5·9; S, 13·4%).

Alkaline hydrolysis. The acid (1 g.) was boiled with 5% sodium hydroxide solution (25 c.c.) for 1 hour. Only a trace of acetophenone was extracted with ether, and the yellow alkaline solution, on acidification, gave an orange precipitate (0·9 g.) which separated from alcohol or from carbon tetrachloride (after several crystallisations) in fine needles, m. p. 107—108° alone or mixed with the original acid.

α-(Benzylthio)propionic Acid (Suter, *Z. physiol. Chem.*, 1895, **20**, 278).—Prepared from benzyl chloride (2·5 g.) and α-mercaptopropionic acid (2·1 g.) as above (but with 1 hour's boiling), the acid (3 g.) crystallised from dilute alcohol in needles, m. p. 77—78° (Suter, *loc. cit.*, gives m. p. 73—74°) (Found : C, 61·6; H, 6·0; S, 16·1. Calc. for $C_{10}H_{12}O_2S$: C, 61·2; H, 6·1; S, 16·3%). The acid was recovered almost unchanged after 1 hour's boiling with 5% sodium hydroxide solution.

α-(α-Benzoylbenzylthio)propionic Acid.—Prepared from α-benzoylbenzyl chloride (4·6 g.) and α-mercaptopropionic acid (2·1 g.) with 1 hour's boiling, the *acid* (5·8 g.), by fractional crystallisation from benzene–light petroleum, yielded two types of crystals : (*a*) needles, m. p. 110—111° (1·8 g.) (Found : C, 67·9; H, 5·5; S, 10·8. $C_{17}H_{16}O_3S$ requires C, 68·0; H, 5·3; S, 10·7%), and (*b*) prisms, m. p. 152—155° (0·8 g.) (Found : C, 67·9; H, 5·4; S, 10·8%). The remainder of the acid remained in the mother-liquors. One form is probably the mixture (DD′ and LL′), and the other the racemic form (DL′ + LD′).

Alkaline hydrolysis. The acid (either form) (2 g.) was hydrolysed as above. The solution became turbid after 3 minutes (cf. comparative experiment on the hydrolysis of the α-thioacetic and β-thiopropionic acids, Schönberg and Iskander, *J.*, 1942, 94), but after 0·5 hour's boiling the cooled turbid solution deposited deoxybenzoin (1·05 g.). The alkaline filtrate, on acidification, gave hydrogen sulphide and a colourless precipitate (0·13 g.) which separated from dilute alcohol in fine needles, m. p. 76—78° alone or mixed with α-(benzylthio)propionic acid (*ca.* 80% C–S fission and *ca.* 20% CO–C fission).

α-(Benzylthio)isobutyric Acid.—Prepared from benzyl chloride (2·5 g.) and α-mercapto*iso*butyric acid (2·4 g.) as above, the acid (4 g.) separated from dilute alcohol in needles, m. p. 96—97° (the m. p. 131° recorded by Larsson and Monies, *Trans. Chalmers Univ. Technol.*, 1945, **47**, 9, has been disproved) (Found : C, 62·6; H, 6·7; S, 15·1. Calc. for $C_{11}H_{14}O_2S$: C, 62·9; H, 6·7; S, 15·2%).

α-(α-Benzoylbenzylthio)isobutyric Acid.—Prepared from the chloride (4·6 g.) and α-mercapto*iso*butyric acid (2·4 g.), the *acid* (6·2 g.) separated from dilute alcohol in needles, m. p. 129—130° (Found : C, 68·6; H, 5·8; S, 10·4. $C_{18}H_{18}O_3S$ requires C, 68·8; H, 5·7; S, 10·2%).

Alkaline hydrolysis. The acid was hydrolysed as above for 0·5 hour. The clear solution finally obtained gave, on acidification, a colourless precipitate which separated from dilute alcohol in needles, m. p. 96—97° alone or mixed with α-(benzylthio)*iso*butyric acid.

α-(Diphenylmethylthio)propionic acid.—Diphenylmethyl bromide (2·5 g.) reacted vigorously with α-mercaptopropionic acid (1·1 g.) with evolution of hydrogen bromide; when the reaction subsided, the mixture was heated at 100° until no more hydrogen bromide was evolved. After cooling, the solid reaction mixture was extracted with sodium hydrogen carbonate solution which on acidification gave the acid (2·6 g.), separating from dilute alcohol in needles, m. p. 144—145° (Found : C, 70·4; H, 6·3; S, 11·9. $C_{16}H_{16}O_2S$ requires C, 70·6; H, 5·9; S, 11·8%).

α-(Diphenylmethylthio)isobutyric Acid.—Prepared from the bromide (2·5 g.) and α-mercapto*iso*butyric acid (1·2 g.), the *acid* (2·7 g.) separated from dilute alcohol in fine needles, m. p. 119—120° (Found : C, 71·6; H, 6·3; S, 10·9. $C_{17}H_{18}O_2S$ requires C, 71·2; H, 6·3; S, 11·2%).

β-(Diphenylmethylthio)propionic Acid.—[Cf. its formation by alkaline hydrolysis of β-(α-benzoyldiphenylmethylthio)propionic acid, Schönberg and Iskander, *loc. cit.*]. Prepared from the bromide (2·5 g.) and β-mercaptopropionic acid (1·1 g.), the acid (2·5 g.) separated from dilute alcohol in fine needles, m. p. 89—90° (Found : C, 71·0; H, 6·0; S, 11·5. Calc. for $C_{16}H_{16}O_2S$: C, 70·6; H, 5·9; S, 11·8%).

This acid, like the two preceding, was recovered almost unchanged after 0·5 hour's boiling with 5% sodium hydroxide solution.

α-(α-Benzoyldiphenylmethylthio)propionic Acid.—α-Benzoyldiphenylmethyl chloride (3·1 g.) and α-mercaptopropionic acid (1·1 g.) in dry toluene (30 c.c.) were boiled for 4 hours until no more hydrogen

chloride was evolved. The solution was then treated with ether and the acid extracted with cold sodium hydroxide solution (2·5%). (The acid is so weak that it could not be extracted with sodium hydrogen carbonate solution.) Acidification gave the acid (3·5 g.) as a viscous mass which could not be solidified or crystallised.

Alkaline hydrolysis. The acid was dissolved in 5% sodium hydroxide solution and boiled for 0·5 hour. Acidification of the resulting clear solution gave a white solid which separated from dilute alcohol in needles, m. p. 144—145° alone or mixed with the α-(diphenylmethylthio)propionic acid.

α-(*α-Benzoyldiphenylmethylthio*)*iso*butyric *Acid.*—Prepared from α-benzoyldiphenylmethyl chloride (3·1 g.) and α-mercapto*iso*butyric acid (1·2 g.), the acid (2·9 g.) was obtained as a viscous mass which could not be solidified or crystallised.

Alkaline hydrolysis. Hydrolysis by 5% sodium hydroxide solution for 0·5 hour gave a white solid which separated from dilute alcohol in needles, m. p. 119—120° alone or mixed with α-(diphenylmethylthio)*iso*butyric acid.

α-(*Triphenylmethylthio*)iso*butyric Acid.*—Triphenylmethyl chloride (2·8 g.) and α-mercapto*iso*butyric acid (1·2 g.) in dry toluene (30 c.c.) were boiled for 2 hours. The *acid* (2·1 g.), isolated as usual, separated from dilute alcohol in small plates, m. p. 155—156° (Found: C, 75·8; H, 6·2; S, 8·8. $C_{32}H_{32}O_2S$ requires C, 76·2; H, 6·1; S, 8·8%).

This acid and α-(triphenylmethylthio)propionic acid (Billmann and Due, *Bull. Soc. chim.*, 1924, **35**, 387) were recovered almost unchanged after 0·5 hour's boiling with 5% sodium hydroxide solution.

α-(p-*Nitrophenyldiphenylmethylthio*)*propionic Acid.*—Prepared from the chloride (3·2 g.) and α-mercaptopropionic acid (1·1 g.) in boiling dry toluene (30 c.c.) (3 hours) and isolated as above, the *acid* (0·5 g.) separated from carbon tetrachloride in very pale yellow needles, m. p. 173—174° (Found: C, 67·2; H, 5·1; N, 4·0; S, 8·6. $C_{22}H_{19}O_4NS$ requires C, 67·2; H, 4·8; N, 3·6; S, 8·1%).

Alkaline hydrolysis. The acid (0·1 g.) was hydrolysed as described above. Turbidity began to appear after the first 5 minutes, and after 15 minutes the liberated oil was extracted from the red liquid with ether and crystallised from light petroleum (b. p. 50—60°) from which it separated in crystals, m. p. 90—94° alone or mixed with an authentic specimen of *p*-nitrotriphenylmethane. Acidification of the alkaline solution gave much hydrogen sulphide.

β-(p-*Nitrotriphenylmethylthio*)*propionic Acid.*—Prepared as above from the chloride (3·2 g.) and β-mercaptopropionic acid (1·1 g.) and isolated in the usual way, the *acid* (0·5 g.) separated from dilute alcohol in pale yellow needles, m. p. 125—126° (Found: N, 3·5; S, 8·2. $C_{22}H_{19}O_4NS$ requires N, 3·6; S, 8·1%).

α-(p-*Nitrotriphenylmethylthio*)iso*butyric Acid.*—Prepared from the chloride (3·2 g.) and α-mercapto*iso*-butyric acid (1·2 g.), the *acid* (0·3 g.) separated from carbon tetrachloride in pale yellow prisms, m. p. 155—156° (decomp.) (Found: N, 3·1. $C_{23}H_{21}O_4NS$ requires N, 3·4%).

The last two acids were recovered almost unchanged after being boiled with 5% sodium hydroxide solution for half an hour. The sodium salts of these two acids are slightly soluble in cold water, and their solutions acquire in sunlight a yellow colour which fades again in the dark.

Neutral Hydrolysis of Tetraphenyldithiodiacetic Acid.—The acid (Becker and Bistrzycki, *Ber.*, 1914, **47**, 3154) was boiled in dry acetone or ethyl methyl ketone for 6 hours; no blue colour was formed and the substance was recovered unchanged; but when it was boiled with acetone or ethyl methyl ketone containing a few drops of distilled water a blue colour was formed. After 6 hours' boiling, the acetone or ethyl methyl ketone was distilled off and the blue residue (thiobenzophenone) extracted with boiling light petroleum (b. p. 60—70°). Remaining in the hydrolysis flask was a solid which after extraction with ether and crystallisation from acetic acid separated as colourless crystals, m. p. 150—152° alone or mixed with authentic thiobenzilic acid (cf. Schöberl, *Ber.*, 1937, **70**, 1188). The ethyl ester of this acid (Becker and Bistrzycki, *loc. cit.*) was recovered almost unchanged after 6 hour's boiling in moist acetone or ethyl methyl ketone and no blue colour was formed. Although the acid dissolves in cold pyridine giving an immediate dark blue colour, the ethyl ester dissolves without producing any colour.

The authors express their gratitude to Professor J. Kenyon, F.R.S., for advice.

FAROUK I UNIVERSITY, FACULTY OF SCIENCE, ALEXANDRIA. [*Received, January 22nd*, 1951.]

455. *The Carbon–Sulphur Fission in Thio-ethers. Part II.* The Retarding Influence of α-Methyl Groups and of the Length of the Acid Chain on the Alkaline Hydrolysis of (Nitrobenzylthio)acetic Acids.*

By Youssef Iskander and Youssef Riad.

The retarding influences of the α-methyl groups and the length of the acid chain on the C–S fission of thio-ethers (Part I) is unable to prevent the alkaline hydrolysis of the corresponding *o*- and *p*-nitrobenzylthio-acids where the *aci*-formation, which is a completed electromeric displacement, has led to the inevitable fission of these thio-ethers. The differences due to the presence of the various retarding factors could not be detected with the *p*-nitro-compounds because of the final transformation of the *p*-nitrobenzyl system into the same substance, *p*-azoxybenzaldehyde, in all the cases examined; but in the cases of the *o*-nitro-compounds the transformation of the *o*-nitrobenzyl system into anthranil, thioanthranil, or *o*-aminobenzaldehyde points to the influence of the retarding factors.

The *m*-nitrobenzylthio-acids were recovered completely unchanged from the alkaline solutions after 15 minutes' boiling, and the *o*- and the *p*-nitro-compounds were rapidly and completely hydrolysed even in the cold. The significance of these results is discussed.

In the preceding paper, the retarding influences of α-methyl groups and the length of the acid chain on the hydrolysis of (2-ketoalkylthio)- and (*p*-nitrotriphenylmethylthio)-acetic acids were clearly traced, and in this research these same retarding structures were attached to the (nitrobenzylthio)acetic acids to ascertain whether they were able to retard the C–S fission to any extent. In the preceding paper it was found that, although (*p*-nitrotriphenylmethylthio)-acetic acid was quickly hydrolysed by alkalis, and the corresponding α-thio-propionic acid required a longer time for its complete hydrolysis, yet the corresponding β-thio-propionic and α-thio-*iso*butyric acid resisted hydrolysis completely. Now it is found that all the corresponding *o*- and *p*-nitrobenzyl compounds can be easily hydrolysed irrespective of all the retarding influences present in the acid chain. The tendency for *aci*-formation in the present case must have led to successive mobilities in the molecule resulting in the inevitable fission of the compound with the transformation of the nitrobenzyl system into an azo-benzoyl system:

$$NO_2{\cdot}C_6H_4{\cdot}CH_2{\cdot} \xrightarrow{-H_2O} [{:}N{\cdot}C_6H_4{\cdot}CO{\cdot}]$$

the final state of which depends upon the mechanism of the reaction and the nature of the medium.

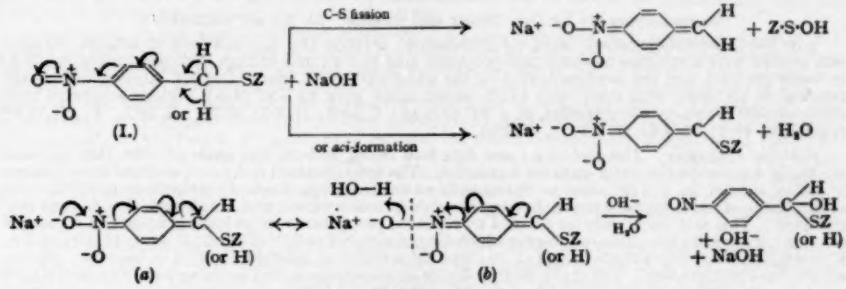
The products of hydrolysis of (*p*-nitrobenzylthio)acetic acid (I; Z = $CH_2{\cdot}CO_2H$) and β-(*p*-nitrobenzylthio)propionic acid (I; Z = $CHMe{\cdot}CO_2H$) by 5 minutes' boiling with 5% alkali (Schönberg and Iskander, *J.*, 1942, 90) were *p*-azobenzaldehyde and *p*-azoxybenzaldehyde, respectively, and the explanation suggested at that time for the production of these two products was simply that the β-sulphenopropionic acid which has oxidising properties could oxidise *p*-azobenzaldehyde (supposed to be initially formed in both cases) to the azoxy-aldehyde in the second case, while in the first case the sulphenoacetic acid, which has no oxidising properties, leaves *p*-azobenzaldehyde unchanged. Now, conversely, it has been shown that the initial product in both reactions is the azoxy-compound and that its formation is independent of the presence of an oxidising agent, since the product of hydrolysis of (*p*-nitrobenzylthio)-acetic acid after only one minute in the hot (or 10 minutes in the cold) was found to be exclusively *p*-azoxybenzaldehyde, and similarly the hydrolysis of α-(*p*-nitrobenzylthio)propionic acid, where the second hydrolysis product "α-sulphenopropionic acid" has no oxidising properties, was found also after 5 minutes' boiling with alkali to be *p*-azoxybenzaldehyde, which on longer boiling (15 minutes) was changed mostly into *p*-azobenzaldehyde. The reduction of the former to the latter aldehyde is therefore due to the sodium sulphide liberated in solution after the decomposition of the sulphenoacetic or α-sulphenopropionic acid, while with β-(*p*-nitrobenzylthio)propionic acid further boiling did not affect the azoxy-

* Part I, preceding paper.

aldehyde because the second product "β-sulphenopropionic acid" did not decompose in solution to give a sulphide ion but changed into the corresponding disulphide, "β-dithiodipropionic acid." In presence of as little sodium sulphide as could be liberated from the decomposition of an equivalent amount of sulphenoacetic acid, the hydrolysis of the propionic acid both in the hot (5 minutes) and in the cold (24 hours) gave *p*-azobenzaldehyde.

The hydrolysis of α-(*p*-nitrobenzylthio)*iso*butyric acid, like that of β-(*p*-nitrobenzylthio)-propionic acid, gave *p*-azoxybenzaldehyde and α-dithiodi*iso*butyric acid.

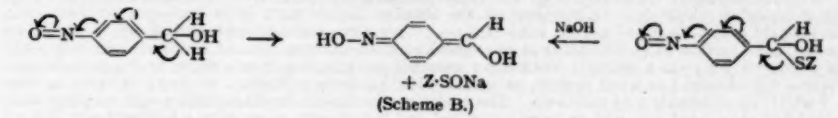
The rearrangement of the *p*-nitrobenzyl system into the azoxy-aldehyde seems to have occurred *via* a *p*-nitroso-alcohol according to scheme A (*o*-nitrotoluene is known to be changed into *o*-nitrosobenzyl alcohol under the influence of alkalis; Kalle & Co., D.R.-P. 194,811; *Chem. Zentr.*, 1908, I, 1345):



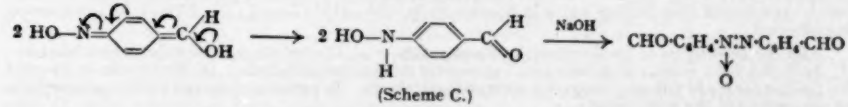
(Scheme A.)

(Z = $CH_2{\cdot}CO_2H$, $CH_2{\cdot}CH_2{\cdot}CO_2H$, $CHMe{\cdot}CO_2H$, or $CMe_2{\cdot}CO_2H$.)

The electronic displacements (*b*) are the results of the attack of the nucleophilic reagent on the α-carbon atom, while those shown in (*a*) are only favoured in acid medium to give the original nitro-compound. The *p*-nitroso-alcohol, being considered as a secondary nitroso-compound, must have rearranged to the more stable oxime (scheme B); this, in turn, can be considered as the imidol type of *p*-hydroxyaminobenzaldehyde which is known to be changed by the action of alkalis into *p*-azoxybenzaldehyde (Alway, *Ber.*, 1903, **36**, 2306) (scheme C):



(Scheme B.)



(Scheme C.)

In parallel with the mechanism suggested above, the final stage in the rearrangement of the *o*-nitrobenzyl system is expected to be anthranil, which is the decomposition product of *o*-nitrosobenzyl alcohol (Bamberger, *ibid.*, p. 839) or of *o*-hydroxyaminobenzaldehyde, which is only known in solution (Bamberger and Elger, *ibid.*, p. 3653). Actually, the alkaline hydrolysis of α-(*o*-nitrobenzylthio)acetic acid gave thioanthranil, while the acidic mother-liquor after being diazotised and boiled with water, gave 5-nitrosalicylic acid, the expected product of the action of excess of nitrous acid on anthranilic acid (cf. Deninger, *J. pr. Chem.*, 1890, **42**, 551) which, in turn, must have been formed after the action of alkalis on the initially expected product of the hydrolysis, *viz.*, anthranil.

The hydrolysis of α-(*o*-nitrobenzylthio)propionic acid gave a steam-volatile liquid which was neither thioanthranil nor *o*-aminobenzaldehyde; this was also obtained in a very pure state from β-(*o*-nitrobenzylthio)propionic acid, while again the hydrolysis of α-(*o*-nitrobenzylthio)*iso*-butyric acid gave a trace of a steam-volatile oil not containing sulphur. The different results obtained from the alkaline hydrolyses of the last four acids point to the influence of

the length of the acid chain or of the presence of α-methyl groups, in that it confers on these compounds different susceptibilities to the attack by the alkali.

Some brownish-red acids, containing nitrogen and sulphur, were isolated from the reaction mixtures after the hydrolyses of all the *o*- and the *p*-nitrobenzylthio-acids investigated, and their structures are still to be investigated.

The *m*-nitrobenzylthio-acids corresponding to the above series of compounds were recovered completely unchanged from the boiling alkaline solutions after 15 minutes, showing that hydrolysis requires to be initiated by electromeric displacements through a conjugated system starting from the influencing group (nitro- or keto-group) and ending at the sulphur atom, a condition which is not satisfied in these *m*-nitro-compounds.

Experimental.

Microanalyses are by Drs. Weiler and Strauss. M. p.s are uncorrected.

α-(p-*Nitrobenzylthio*)*propionic Acid.*—*p*-Nitrobenzyl chloride (4·3 g.), dissolved in alcohol (70 c.c.), was treated with a solution of α-mercaptopropionic acid (2·7 g.) and sodium hydrogen carbonate (5 g.) in water (20 c.c.), and the mixture heated on the water-bath for 1 hour. Cooling, dilution with water, removal of turbidity with ether, and finally acidification gave an *acid* (4·5 g.) which separated from dilute alcohol in creamy white needles, m. p. 92° (Found : C, 50·3; H, 4·7; N, 5·8; S, 13·7. $C_{10}H_{11}O_4NS$ requires C, 49·8; H, 4·6; N, 5·8; S, 13·3%).

Alkaline hydrolysis. The acid (5 g.) was dissolved in 5% sodium hydroxide solution (125 c.c.) and gradually warmed on the water-bath for 3 minutes. The solid obtained (1·6 g.) crystallised from benzene in yellow needles, m. p. 190° alone or mixed with an authentic specimen of *p*-azoxybenzaldehyde. On acidification of the alkaline filtrate, hydrogen sulphide was evolved and a red acid (1·5 g.) was precipitated. This acid could only be purified by repeated precipitation from sodium hydrogen carbonate solution; it formed a brownish-red powder which did not melt below 350° (Found : C, 54·0; H, 4·3; N, 5·0; S, 10·4%), and was very soluble in cold alcohol and hot acetic acid, insoluble in ether or benzene; its constitution is still unknown. The acidic mother-liquor on diazotisation and coupling with β-naphthol gave a red dye, and when diazotised and boiled with water gave a hydroxy-acid (0·1 g.) which crystallised from dilute alcohol in creamy white needles, m. p. 245—247° (Found : N, 7·7%); its constitution is unknown. The hydrolysis was repeated with 15 minutes' boiling; the solid obtained was extracted with hot benzene which gave a small amount of *p*-azoxybenzaldehyde, while the residue crystallised from acetic acid in orange-red crystals, m. p. 230—235° alone or mixed with an authentic specimen of *p*-azobenzaldehyde.

α-(p-*Nitrobenzylthio*)*iso*butyric *Acid.*—Prepared from *p*-nitrobenzyl chloride (4·3 g.) and α-mercapto-*iso*butyric acid (3 g.) and isolated as described above, the *acid* (4·5 g.) crystallised from dilute alcohol in pale yellow needles, m. p. 145—146° (Found : C, 52·1; H, 5·2; N, 5·4; S, 12·2. $C_{11}H_{13}O_4NS$ requires C, 51·8; H, 5·1; N, 5·5; S, 12·5%).

Alkaline hydrolysis. The acid (5 g.) was hydrolysed as described above. The solid obtained (1·2 g.) was *p*-azoxybenzaldehyde. Acidification of the alkaline filtrate gave little hydrogen sulphide with the gradual precipitation of a dark solid (1·5 g.). This was extracted with boiling water which, on cooling, gave leaflets, m. p. 197° alone or mixed with an authentic specimen of α-dithiodi*iso*butyric acid; the residue (0·2 g.) was a red acid which after repeated precipitation from sodium hydrogen carbonate solution was obtained as a red powder, m. p. 127—130° (decomp.) (Found : C, 54·9; H, 4·9; N, 7·6; S, 9·6%); its constitution is unknown. The acidic mother-liquor on diazotisation and coupling with β-naphthol gave a red dye, and on being diazotised and boiled with water gave a hydroxy-acid (0·1 g.) which crystallised from boiling water in needles, m. p. 207—213° (Found : N, 7·7%); its constitution is unknown.

Alkaline Hydrolysis of (p-*Nitrobenzylthio*)*acetic Acid.*—(*a*) Hydrolysis (cf. Schönberg and Iskander, *J.*, 1942, 90) for 1 minute in boiling alkali gave only *p*-azoxybenzaldehyde. (*b*) Hydrolysis in the cold for 1 minute or for 10 minutes also gave *p*-azoxybenzaldehyde. Repetition of (*a*) and (*b*) in an atmosphere of nitrogen gave the same results.

Alkaline Hydrolysis of β-(p-*Nitrobenzylthio*)*propionic Acid in the Presence of Sodium Sulphide* (cf. Schönberg and Iskander, *loc. cit.*).—The acid (2 g.) was dissolved in 5% sodium hydroxide solution (50 c.c.) containing sodium sulphide (0·65 g.), and the mixture (*a*) boiled for 5 minutes, or (*b*) left for 24 hours in the cold. The product in both cases was *p*-azobenzaldehyde.

A suspension of *p*-azoxybenzaldehyde (1·1 g.) in 5% sodium hydroxide solution (50 c.c.) containing sodium sulphide (0·65 g.) was boiled for 5 minutes; reduction to *p*-azobenzaldehyde was complete.

(m-*Nitrobenzylthio*)*acetic Acid.*—Prepared from *m*-nitrobenzyl chloride (4·3 g.) and mercaptoacetic acid (2·5 g.) and isolated as above, the *acid* (4·5 g.) crystallised from dilute alcohol in creamy white needles, m. p. 81—82° (Found : C, 47·4; H, 4·2; N, 6·6; S, 14·5. $C_9H_9O_4NS$ requires C, 47·6; H, 4·0; N, 6·2; S, 14·1%).

β-(m-*Nitrobenzylthio*)*propionic Acid.*—Prepared from the chloride (4·3 g.) and mercapto-acid (2·7 g.) as above, the *acid* (5 g.) crystallised from dilute alcohol in creamy white needles, m. p. 99° (Found : C, 50·2; H, 4·7; N, 6·0; S, 13·6. $C_{10}H_{11}O_4NS$ requires C, 49·8; H, 4·6; N, 5·8; S, 13·3%).

α-(m-*Nitrobenzylthio*)*propionic Acid.*—Prepared from the chloride (4·3 g.) and mercapto-acid (2·7 g.) as above, the *acid* (4·6 g.) crystallised from dilute alcohol in creamy white needles, m. p. 82° (Found : C, 50·0; H, 4·7; N, 5·9; S, 13·8. $C_{10}H_{11}O_4NS$ requires C, 49·8; H, 4·6; N, 5·8; S, 13·3%).

α-(m-*Nitrobenzylthio*)*isobutyric Acid.*—Prepared from the chloride (4·3 g.) and mercapto-acid (3 g.) as above, the *acid* (4·6 g.) crystallised from dilute alcohol in creamy white needles, m. p. 93° (Found: C, 51·7; H, 5·2; N, 5·3; S, 11·7. $C_{11}H_{13}O_4NS$ requires C, 51·8; H, 5·1; N, 5·5; S, 12·5%).

The four *m*-nitrobenzylthio-acids were recovered unchanged after 15 minutes' boiling with 5% sodium hydroxide solution.

(o-*Nitrobenzylthio*)*acetic acid.*—Prepared from the chloride (Holleman, *Rec. Trav. chim.*, 1914, **33**, 15; b. p. 118°/1·5 mm., 125°/4·0 mm.) (4·3 g.) and mercaptoacetic acid (2·5 g.) as above, the *acid* (4·5 g.) crystallised from dilute alcohol in creamy white scales, m. p. 98—99° (Found: C, 47·7; H, 3·9; N, 5·8; S, 13·5. $C_9H_9O_4NS$ requires C, 47·6; H, 4·0; N, 6·2; S, 14·1%).

Alkaline hydrolysis. A solution of the acid (5 g.) in 5% sodium hydroxide solution (125 c.c.) was distilled until the distillate was no longer turbid. Extraction of the distillate with ether gave a pale yellow oil (0·25 g.) which contained nitrogen and sulphur and gave with an alcoholic solution of mercuric chloride a double compound, m. p. 210° alone or mixed with that from authentic thioanthranil (Bamberger, *Ber.*, 1909, **42**, 1667). Other experiments to prove the identity of the oil as thioanthranil were all positive (cf. Gabriel and Leupold, *Ber.*, 1898, **31**, 2186).

Acidification of the alkaline solution remaining from the hydrolysis gave hydrogen sulphide and a small amount of sulphur dioxide with gradual precipitation of a red sticky mass which when shaken with sodium hydrogen carbonate solution and ether dissolved partly among the two layers, leaving a very small amount of a neutral substance containing nitrogen and sulphur. Evaporation of the ethereal layer left free sulphur; the hydrogen carbonate layer after acidification gave a brownish-red acid (0·5 g.) which after repeated precipitation from carbonate solution was further purified by precipitation from an alcoholic solution by the addition of excess of ether as a brownish-red powder, m. p. 193—197° (decomp.) (Found: C, 52·1; H, 4·1; N, 6·3; S, 7·1%); its constitution is unknown. The acidic mother-liquor, after the isolation of the red sticky mass, on diazotisation and coupling with β-naphthol gave a red dye and on being diazotised and boiled with water gave a hydroxy-acid (0·9 g.) which crystallised from hot water in needles, m. p. 226—227° alone or mixed with authentic 5-nitrosalicylic acid (Deninger, *J. pr. Chem.*, 1890, **42**, 551).

α-(o-*Nitrobenzylthio*)*propionic Acid.*—Prepared from the chloride (4·3 g.) and mercapto-acid (2·7 g.) as above, the *acid* (5 g.) crystallised from dilute alcohol in pale yellow prisms, m. p. 124—125° (Found: C, 49·8; H, 4·7; N, 5·8; S, 13·1. $C_{10}H_{11}O_4NS$ requires C, 49·8; H, 4·6; N, 5·8; S, 13·3%).

Alkaline hydrolysis. The acid (5 g.) was hydrolysed as described above. The volatile oil (0·15 g.) did not contain sulphur but had an odour of anthranil. It gave a picrate, m. p. 233—237°, and a mercuric chloride compound, m. p. (rapid heating) 180—185° (no melting on slow heating). On being diazotised and boiled with water it gave a phenol which crystallised from dilute alcohol in pale yellow needles (Found: C, 50·3; H, 3·0; N, 7·8. Calc. for $C_7H_7O_2N$: C, 50·3; H, 3·0; N, 8·4%), m. p. 121—122° alone or mixed with authentic 5-nitrosalicylaldehyde, m. p. 126° (Miller, *Ber.*, 1887, **20**, 1929). The oil has not yet been identified.

Acidification of the alkaline solution remaining after hydrolysis gave hydrogen sulphide and a little sulphur dioxide with the gradual precipitation of a brownish-red sticky mass (0·7 g.) which, on treatment as previously, left in the ethereal layer a small amount of sulphur, while the hydrogen carbonate layer, on acidification, gave a dark brownish-red acid (0·5 g.), soluble in cold alcohol or hot glacial acetic acid, insoluble in ether or benzene. It was obtained after repeated precipitation from carbonate solution as a brown powder, m. p. 104—105° (decomp.) (Found: C, 59·6; H, 4·2; N, 8·1; S, 6·2%); its constitution is unknown. The acidic mother-liquor, after isolation of the red sticky mass, on diazotisation and coupling with β-naphthol gave a red dye, and when diazotised and boiled with water gave a hydroxy-acid (1·1 g.) which crystallised from dilute alcohol in needles, m. p. 235° which gave a deep violet with ferric chloride (Found: N, 7·3%); its structure is unknown.

β-(o-*Nitrobenzylthio*)*propionic Acid.*—Prepared from the chloride (4·3 g.) and mercapto-acid (2·7 g.) as above, the *acid* (5 g.) crystallised from dilute alcohol in pale yellow needles, m. p. 77—78° (Found: C, 49·4; H, 4·7; N, 6·0; S, 13·2. $C_{10}H_{11}O_4NS$ requires C, 49·8; H, 4·6; N, 5·8; S, 13·3%).

Alkaline hydrolysis. The acid (5 g.) was hydrolysed as described above. The volatile substance (0·6 g.) solidified immediately in silvery scales, m. p. 39—40° alone or mixed with authentic *o*-aminobenzaldehyde (*Helv. Chim. Acta*, 1935, **18**, 1235). Its mercuric chloride compound (Friedländer, *Ber.*, 1882, **15**, 2572) crystallised from dilute alcohol in needles, m. p. (rapid heating) 135—140° or (slow heating) 209—210°. On diazotisation of *o*-aminobenzaldehyde in hydrochloric acid solution and boiling with water, the solution, after cooling, precipitated a phenol which crystallised from dilute alcohol in yellow needles, m. p. 118—120° (Found: C, 50·2; H, 3·2; N, 8·5. Calc. for $C_7H_7O_2N$: C, 50·3; H, 3·0; N, 8·5%). The mixed m. p. with authentic 5-nitrosalicylaldehyde of m. p. 126° gave no depression.

Acidification of the alkaline solution remaining from the hydrolysis liberated small amounts of hydrogen sulphide and sulphur dioxide, with the gradual precipitation of a brown sticky mass (0·4 g.) which on treatment as above gave a brown acid (0·3 g.), soluble in cold alcohol or hot acetic acid, insoluble in ether or benzene. It was obtained after repeated precipitation from carbonate solution as a black powder, m. p. 165° (decomp.) (Found: C, 56·3; H, 4·0; N, 7·9; S, 12·3%); its constitution is unknown.

The acidic mother-liquor, after separation of the brown sticky mass, on diazotisation and coupling with β-naphthol gave a red dye, and on diazotisation and boiling with water gave a hydroxy-acid (0·8 g.) which crystallised from dilute alcohol in fine needles, m. p. 200—208°, and gave a deep violet-red colour with ferric chloride (Found: N, 7·1%); its constitution is still unknown.

α-(o-*Nitrobenzylthio*)*isobutyric Acid.*—Prepared from the chloride (4·3 g.) and mercapto-acid (3 g.) as above, the *acid* (5 g.) crystallised from dilute alcohol in pale yellow needles, m. p. 90—91° (Found: C, 52·0; H, 5·2; N, 5·4; S, 12·7. $C_{11}H_{13}O_4NS$ requires C, 51·8; H, 5·1; N, 5·5; S, 12·5%).

Alkaline hydrolysis. The acid (5 g.) was hydrolysed as described earlier. The volatile substance consisted of a slight trace of an oil containing no sulphur, with an odour of anthranil. It gave a picrate and a mercuric chloride compound. Acidification of the residual alkaline solution liberated a small amount of hydrogen sulphide with the gradual precipitation of a red sticky mass (0·6 g.) which on similar treatment as before gave a brown acid (0·5 g.), insoluble in ether or benzene, soluble in cold alcohol or hot glacial acetic acid. Repeated precipitation from carbonate solutions gave a dark brown powder, m. p. 85—100° (decomp.); its constitution is unknown. The acid chloride, prepared from the acid and thionyl chloride as a dark red viscous mass was treated with absolute alcohol, and the resulting ethyl ester separated from carbon tetrachloride–light petroleum as a brown powder, m. p. 180—185° (Found: C, 57·6; H, 4·2; N, 7·5; S, 5·6%).

The acidic mother-liquor on diazotisation and coupling with β-naphthol gave a red dye, and on diazotisation and boiling gave a hydroxy-acid (0·6 g.) which crystallised from dilute alcohol in needles, m. p. 186—205°, and gave a deep violet-red colour with ferric chloride (Found: N, 7·8%); its constitution is unknown.

The authors express their gratitude to Professor J. Kenyon, F.R.S., for his valuable advice.

FAROUK I UNIVERSITY, FACULTY OF SCIENCE,
ALEXANDRIA.

[*Received, January 22nd,* 1951.]

---

456. *The Carbon–Sulphur Fission in Thio-ethers. Part III.* The Retarding Influence of the Length of the Radical Chain and of a Second α-Thio-acetic Acid Group on the Alkaline Hydrolysis of (Nitrobenzylthio)- and (Nitrodiphenylmethylthio)-acetic Acids.*

By YOUSSEF ISKANDER and ADIB SALAMA.

The action of alkalis on (*p*-nitrodiphenylmethylthio)acetic acid (cf. I) and (*p*-nitrodiphenylmethylenedithio)diacetic acid (cf. II) gives *p*-azoxybenzophenone, whereas that on (*p*-nitrobenzylidenedithio)diacetic (III) and (2-*p*-nitrophenylethylthio)acetic acid effected, not a C–S fission, but the formation of *aci*-structures leading to secondary products which are brownish-red acids still containing nitrogen and sulphur. Further, while (*m*-nitrobenzylthio)acetic acid (see Part II) is completely unchanged by alkalis, the *m*-nitro-compounds of the present series of acids, although they likewise do not suffer a C–S fission, nevertheless undergo secondary changes leading to the formation of brownish-red acids again still containing nitrogen and sulphur, thus showing the influence of the additional phenyl and α-thioacetic acid groups in this respect. The significance of these results is discussed.

THE retarding influences on the alkaline hydrolyses of thio-ethers which are discussed in this paper, namely, (*a*) the substitution of α-hydrogen atoms of the nitrobenzyl radical in (*p*- and *m*-nitrobenzylthio)acetic acids by a phenyl group or a second thioacetic acid group or by both

$NO_2 \cdot C_6H_4 \cdot CHPh \cdot SZ$ $NO_2 \cdot C_6H_4 \cdot CH(SZ)_2$ $NO_2 \cdot C_6H_4 \cdot CPh(SZ)_2$ ($Z = CH_2 \cdot CO_2H$.)

and (*b*) the interruption of conjugation of the nitro-group with the sulphur atom by a CH_2 group ($NO_2 \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot SZ$), were applied so as to throw further light on the mechanism of the C–SZ fission in these and similar structures, and to decide whether the presence of one or of the two α-hydrogen atoms in the nitrobenzyl group is necessary for the formation of the azoxy-carbonyl system finally obtained.

Hydrolysis of (*p*-nitrobenzylthio)acetic acid (see Part II) and (*p*-nitrodiphenylmethylthio)-acetic acid (cf. I), which differ only by a phenyl group in the α-position, led to *p*-azoxybenzaldehyde and *p*-azoxybenzophenone, respectively. This result shows that the presence of only one hydrogen atom in the α-position sufficed for the formation of the azoxy-carbonyl system, and accordingly, in the case of (*p*-nitrobenzylthio)acetic acid, one of the two α-hydrogen atoms cannot have been involved in the mechanism of the formation of *p*-azoxybenzaldehyde. The formation of *p*-azoxybenzophenone, on the lines suggested for the formation of *p*-azoxybenzaldehyde through an intermediate stage of *p*-hydroxylaminobenzaldehyde

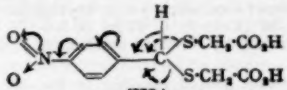
* Part II, preceding paper.

(Part II), might have taken place also *via* the formation of *p*-hydroxylaminobenzophenone (an unknown compound), and whether the C–SZ fission or the *aci*-formation preceded the other on the first attack of the alkali could not be proved; but in the sodium salt of (*p*-nitrodiphenylmethylenedithio)diacetic acid (cf. II), where no α-hydrogen atom is present, the only possibility for the relay of the electromeric displacements towards the powerful electron-attractive nitro-group under the influence of the alkali was one C–SZ fission resulting in the formation of (I):

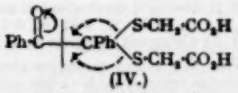
$$\underset{\text{(II.)}}{NO_2\cdot C_6H_4\cdot CPh(S\cdot CH_2\cdot CO_2Na)_2} \xrightarrow{NaOH} \underset{\text{(I.)}}{NO_2\cdot C_6H_4\cdot CHPh\cdot S\cdot CH_2\cdot CO_2Na} + NaO\cdot S\cdot CH_2\cdot CO_2Na$$

which, in turn, was converted into *p*-azoxybenzophenone as before. The sulphide ion (after the decomposition of the liberated sulphenoacetic acid molecule) did not convert *p*-azoxy- into *p*-azo-benzophenone (contrast the case of *p*-azoxybenzaldehyde).

The C–SZ fission, however, was completely prevented in the case of (*p*-nitrobenzylidenedithio)diacetic acid (III). The product, although different from the starting material and still unidentified, was again a brownish-red acid containing nitrogen and sulphur. Had the C–S fission occurred first in this compound, the final product could have been *p*-azobenzaldehyde through the prior formation of (*p*-nitrobenzylthio)acetic acid (cf. Part II). *aci*-Formation must therefore have been the quicker process occurring in this compound. Both sulphur atoms must have contributed equally in the electromeric displacements towards the nitro-group, so that neither atom becomes sufficiently deficient in electrons to allow C–S cleavage to be faster than the *aci*-formation. The same explanation is applicable to the case of the acid (IV), where the C–S fission is also prevented by elimination of the benzoyl group (Behaghel and Schneider, *Ber.*, 1935, **68**, 1588):



(III.)

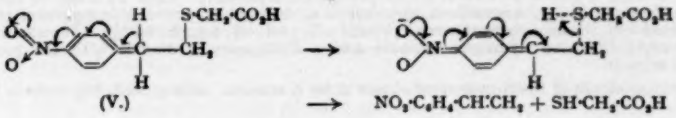


(IV.)

The non-nitro-compounds corresponding to the above series of thio-ethers, as well as the corresponding *m*-nitro-compounds, did not suffer a C–S fission, although the latter compounds were converted into nitrogen- and sulphur-containing unidentified acids. That from (*m*-nitrodiphenylmethylthio)acetic acid differed from the starting material only in being red, both being viscous liquids giving the same analytical data; on the other hand, the resinous acids from *m*-nitrobenzylidenedithiodiacetic acid and *m*-nitrodiphenylmethylenedithiodiacetic acid differed from their starting materials in their analytical data. Since (*m*-nitrobenzylthio)acetic acid did not suffer such a change (cf. Part II), it seems that the additional phenyl or α-thioacetic acid group was responsible for unexplained changes.

The interruption of conjugation of the nitro-group with the sulphur atom by a CH_2 group in α-(2-*p*-nitrophenylethylthio)acetic acid (V) has also prevented the C–S fission, and again *aci*-formation must have occurred, as indicated by the formation of a brownish-red acid containing both nitrogen and sulphur. A side reaction in the hydrolysis of (V) is the formation of a very small amount of *p*-nitrostyrene, a reaction which occurs *only* in neutral medium, most of the acid being recovered unchanged. This side reaction is similar to the main decomposition reaction of $Ph\cdot CO\cdot CH_2\cdot CHPh\cdot S\cdot CH_2\cdot CO_2H$, which gives benzoylstyrene and thioglycollic acid (Behaghel and Ratz, *Ber.*, 1939, **72**, 1257).

The corresponding (2-*m*-nitrophenylethylthio)acetic acid, prepared from *m*-nitrostyrene and mercaptoacetic acid in presence of ascaridole (cf. the general method of preparation of similar compounds, Kharasch and Mayo, *Chem. and Ind.*, 1938, 752), although only obtained as an impure viscous oil, was recovered unchanged from the alkaline medium after 15 minutes' boiling, thus pointing to the influence of the *p*-nitro-group in initiating the partial decomposition of (V) into *p*-nitrostyrene, a reaction which does not occur either with the non-nitro- or the *m*-nitro-compound:



Experimental.

Microanalyses are by Drs. Weiler and Strauss, Oxford. M. p.s are uncorrected.

(p-*Nitrodiphenylmethylthio*)*acetic Acid.*—*p*-Nitrodiphenylmethanol (Lund., *Ber.*, 1937, **70**, 1520) (5 g.) and mercaptoacetic acid (3 g.) were heated together at 110° while dry hydrogen chloride was passed into the molten mixture for 1 hour. Cooling, treatment with sodium hydrogen carbonate solution, filtration to remove unchanged alcohol (0·3 g.), and finally acidification gave an oil which solidified in the ice-chest to a pale yellow *acid* (6·3 g.) which separated from benzene in prisms (6·1 g.), m. p. 127—128° (Found: C, 59·9; H, 4·4; N, 4·7; S, 10·4. $C_{15}H_{13}O_4NS$ requires C, 59·3; H, 4·4; N, 4·6; S, 10·5%).

Alkaline hydrolysis. The acid (2 g.) dissolved in cold 5% sodium hydroxide solution (20 c.c.) with the formation of a clear yellow colour which gradually changed to deep orange-red. After 15 minutes at room temperature turbidity began to appear, and after 24 hours a solid cake was formed in the dark solution. Dilution with water, filtration, and washing with water gave a deep orange, solid p-*azoxybenzophenone* (1·4 g.) which crystallised from acetic acid as golden yellow shining plates, m. p. 200° (Found: C, 76·8; H, 4·6; N, 7·2%; *M*, 410. $C_{26}H_{18}O_3N_2$ requires C, 76·8; H, 4·5; N, 6·9%; *M*, 406). *p*-Azoxybenzophenone is recorded as being formed, together with *p*-azobenzophenone, by the alkaline reduction of *p*-nitrobenzophenone but could not be isolated from the mixture which was reduced as a whole by alcoholic ammonium sulphide to *p*-hydrazobenzophenone which, in turn, could be oxidised by mercuric oxide to pure azobenzophenone, m. p. 219° (Carré, *Compt. rend.*, 1907, **144**, 34; *Bull. Soc. chim.*, 1909, **5**, 277). The pure *p*-azoxybenzophenone obtained on hydrolysis of our acid could be similarly changed through the same steps into *p*-azobenzophenone, m. p. 219° (Found: C, 79·5; H, 4·7; N, 7·6%; *M*, 393. Calc. for $C_{26}H_{18}O_2N_2$: C, 79·9; H, 4·6; N, 7·2%; *M*, 390).

Acidification of the deep-red alkaline filtrate after the hydrolysis caused decolourisation, with the evolution of hydrogen sulphide and a little sulphur dioxide and the precipitation of colloidal sulphur.

The same hydrolysis products were obtained by 5 minutes' boiling with 5% sodium hydroxide solution.

(m-*Nitrodiphenylmethylthio*)*acetic Acid.*—*m*-Nitrodiphenylmethanol, prepared by Meerwein–Ponndorf reduction (Lund, *loc. cit.*) of *m*-nitrobenzophenone in almost theoretical yield, crystallises from light petroleum (b. p. 60—80°) in clusters of needles, m. p. 68—70° (Found: C, 67·9; H, 5·0; N, 6·3. Calc. for $C_{13}H_{11}O_3N$: C, 68·3; H, 4·8; N, 6·1%) (cf. its preparation by Newman and Smith, *J. Org. Chem.*, 1948, **13**, 592, by Grignard reagents at −70°).

The alcohol (8 g.) and mercaptoacetic acid (3·2 g.) were heated together at 80—90° while dry hydrogen chloride was passed into the molten mixture for 1½ hours. Treatment as for the *p*-isomer gave an oil (9 g.) which did not solidify in the ice-chest and could neither be distilled under reduced pressure nor crystallised. After repeated liberation from sodium hydrogen carbonate solution, extraction with ether, and boiling of the ethereal solutions with charcoal, the *acid* was obtained as a viscous colourless liquid (Found: C, 59·3; H, 4·7; N, 4·3; S, 9·7. $C_{15}H_{13}O_4NS$ requires C, 59·3; H, 4·4; N, 4·6; S, 10·5%).

Alkaline hydrolysis. The clear yellow solution of the acid (2 g.) in 5% sodium hydroxide solution (20 c.c.) acquired a brownish-red colour after 5 minutes' boiling, but no precipitate was formed. On acidification a trace of hydrogen sulphide was detected while the liberated brownish-red oily acid, after liberation from sodium hydrogen carbonate solution and boiling of the ethereal extracts with charcoal several times, was obtained as a red viscous oil (1·7 g.), analysis of which (Found: C, 59·7; H. 4·5; N, 4·6; S, 10·5%) still agrees closely with that of the original acid.

(Diphenylmethylthio)acetic acid, m. p. 128—130° (Holmberg, *J. pr. Chem.*, 1934, **141**, 93; Behaghel and Ratz, *Ber.*, 1939, **72**, 1275), was recovered almost unchanged after 0·5 hour's boiling with 5% sodium hydroxide solution.

(p-*Nitrodiphenylmethylenedithio*)*diacetic Acid.*—(*a*) *p*-Nitrobenzophenone (10 g.) and mercaptoacetic acid (10 g.) were heated together on the water-bath with passage of dry hydrogen chloride for 5 hours. The usual treatment afforded unchanged *p*-nitrobenzophenone (6 g.) and a viscous substance (12 g.) from which, after extraction with ether and crystallisation from benzene–alcohol, the *acid* separated in aggregates of needles (6·5 g.), m. p. 169—170° (Found: C, 51·7; H, 3·9; N, 3·7; S, 16·4. $C_{17}H_{15}O_4NS_2$ requires C, 51·9; H, 3·8; N, 3·6; S, 16·3%). Passage of dry hydrogen chloride for 1 hour only gave a 33% yield.

(*b*) Heating a mixture of *p*-nitrobenzophenone dichloride (6·5 g.) and mercaptoacetic acid (4·1 g.) on the water-bath until no more hydrogen chloride was evolved and then isolation of the products as described above gave only 2·3 g. (27·2%) of the acid.

(*c*) Heating a mixture of *p*-nitrobenzophenone (10 g.) and mercaptoacetic acid (8 g.) in presence of freshly fused and powdered zinc chloride (2·5 g.) for 2 hours (cf. Bongartz, *Ber.*, 1888, **21**, 478) gave only 2 g. (12%) of the pure acid.

Alkaline hydrolysis. The acid (2 g.) dissolved in 5% sodium hydroxide solution (20 c.c.) with the formation of a clear yellow colour which changed after a few seconds to deep yellow and then to brown; during 10 minutes a yellow flocculent sticky precipitate separated. After 24 hours in the cold the precipitate obtained (0·8 g.) crystallised from acetic acid in golden-yellow shining plates, m. p. 200° alone or mixed with the azoxybenzophenone (Found: C, 76·9; H, 4·5; N, 6·9%). The alkaline filtrate, on acidification, liberated hydrogen sulphide and a little sulphur dioxide with the precipitation of colloidal sulphur.

The same products of hydrolysis were obtained by 5 minutes' boiling with 5% sodium hydroxide solution.

(m-*Nitrodiphenylmethylenedithio*)*diacetic acid.*—Dry hydrogen chloride was passed into a molten mixture of *m*-nitrobenzophenone (10 g.) and mercaptoacetic acid (8 g.) on the water-bath for 1 hour. This afforded unchanged *m*-nitrobenzophenone (3·5 g.) and a very viscous dark sticky material (9·3 g.) from which the acid was obtained, after crystallisation from benzene–alcohol, as clusters of needles (5 g.), m. p. 159—160° (Found: C, 52·0; H, 3·8; N, 3·7; S, 16·5. $C_{17}H_{15}O_6NS_2$ requires C, 51·9; H, 3·8; N, 3·6; S, 16·3%).

Alkaline hydrolysis. A solution of the acid (4 g.) in 5% aqueous sodium hydroxide (50 c.c.) at room temperature gave, after 26 hours, no precipitate, whilst acidification of the resulting deep red solution liberated very little sulphur dioxide with the precipitation of a dark brown sticky material (3 g.). Boiling this with benzene removed unchanged acid, and repeated precipitation from sodium hydrogen carbonate solutions then yielded a dark brown solid, m. p. 185—190° (decomp.) (Found: C, 61·7; H, 3·7; N, 3·6; S, 12·4%), very soluble in pyridine or aniline, hardly soluble in alcohol or ether.

(*Diphenylmethylenedithio*)*diacetic Acid.* Bongartz's method (*loc. cit.*) gave a very poor yield of this acid. This author reports failure with the following method which we found to give the best yield: Dry hydrogen chloride was passed into a mixture of benzophenone (2 g.) and mercaptoacetic acid (2 g.) at 110° for 2 hours. Isolated as described above, the acid (3 g.) crystallised from dilute acetic acid in shiny plates, m. p. 162—163° [m. p.s recorded are 163—164° (*Ber.*, 1886, **19**, 1931) and 175—176° (*Ber.*, 1888, **21**, 478)].

The acid (1 g.) was recovered almost unchanged (m. p. 166°; 0·8 g.) after 0·5 hour's boiling with 5% sodium hydroxide solution.

(p-*Nitrobenzylidenedithio*)*diacetic Acid.*—The foregoing method was superior to that of Bongartz (*loc. cit.*). Prepared from *p*-nitrobenzaldehyde (10 g.) and mercaptoacetic acid (12 g.) on the water-bath with passage of dry hydrogen chloride for 1 hour, the pure acid (12·5 g.), formed glistening needles (from water), m. p. 161—162°.

Alkaline hydrolysis. The acid (5 g.) dissolved in cold 5% sodium hydroxide solution (50 c.c.) with the formation of a deep red solution in the course of few seconds, but after 5 minutes' boiling no precipitate was produced. Acidification gave a little hydrogen sulphide and a dark brown solid. Boiling water removed from this any unchanged acid, and repeated precipitation from sodium hydrogen carbonate solution yielded an acid as a dark brown-red powder which did not melt but decomposed above 350° (Found: C, 54·8; H, 3·9; N, 8·4; S, 18·8%), insoluble in most of the organic solvents, freely soluble in cold pyridine or aniline.

The same result was obtained by carrying out the reaction at room temperation for 24 hours.

(m-*Nitrobenzylidenedithio*)*diacetic Acid.*—This was obtained in good yield and quality by Bongartz's method (*loc. cit.*) or by using hydrogen chloride as the condensing agent as described above. The crude acid (19·4 g.) obtained from *m*-nitrobenzaldehyde (10 g.) and mercaptoacetic acid (12 g.) separated from chloroform in colourless needles, m. p. 130—131°.

Alkaline hydrolysis. The acid (3 g.) dissolved in cold 5% sodium hydroxide solution (30 c.c.) with the formation of a clear brownish-red solution, which, after 5 minutes' boiling, gave no precipitate. Acidification gave very little hydrogen sulphide and a very dark brown tarry substance which did not solidify in the ice-chest but after repeated precipitation from sodium hydrogen carbonate solution and storage in a desiccator for 24 hours gave an acid as a dark brown-red powder (2·2 g.), m. p. 85—90° (decomp.) (Found: C, 46·8; H, 3·7; N, 4·7; S, 19·7%), partly soluble in hot alcohol or hot acetic acid, freely soluble in cold pyridine or aniline.

(Benzylidenedithio)diacetic acid (Bongartz, *loc. cit.*) was recovered almost unchanged after 0·5 hour's boiling with 5% sodium hydroxide solution.

(2-p-*Nitrophenylethylthio*)*acetic Acid.*—2-*p*-Nitrophenylethyl chloride (10 g.) (Barger, *J.*, 1909, **95**, 2194) in alcohol (50 c.c.) was treated with a solution of mercaptoacetic acid (5 g.) and sodium hydrogen carbonate (9·2 g.) in water (40 c.c.), and the mixture boiled on the water-bath for 1 hour. Cooling, dilution with water, filtration, and acidification gave a yellow oil which solidified (11·2 g.) in the ice-chest. Crystallisation from carbon tetrachloride gave colourless scales of the *acid*, m. p. 85° (Found: C, 49·7; H, 4·7; N, 5·8; S, 13·3. $C_{10}H_{11}O_4NS$ requires C, 49·7; H, 4·6; N, 5·8; S, 13·3%).

Alkaline hydrolysis. The acid (8 g.) in 5% sodium hydroxide solution (200 c.c.) was boiled under reflux for 5 minutes. The deep red solution was steam-distilled until no further turbidity appeared in the distillate. The volatile *p*-nitrostyrene solidified in the ice-chest as crystals of m. p. 21° (Basler, *Ber.*, 1883, **16**, 3007, reported m. p. 29°; Strassburg, Gregg, and Walling, *J. Amer. Chem. Soc.*, 1947, **69**, 2141, reported m. p. 21·4°) which on treatment with bromine in ether gave the pale yellow dibromide (Basler, *loc. cit.*), m. p. 72° [from light petroleum (b. p. 50—60°)] (Found: 31·3; H, 2·6; N, 5·1; Br, 51·5. Calc. for $C_8H_7O_2NBr_2$: C, 31·1; H, 2·3; N, 4·5; Br, 51·7%). The alkaline steam-distillation residue, on acidification, gave hydrogen sulphide and a brown gelatinous precipitate; boiling this with carbon tetrachloride to remove any unchanged acid, and repeated precipitation from sodium hydrogen carbonate solution, gave a brownish-red powder (6·9 g.) which did not melt but decomposed above 350° (Found: C, 56·8; H, 4·5; N, 6·2; S, 9·9%). The same products were obtained by hydrolysis at ordinary temperature during 24 hours.

Hydrolysis in neutral medium. A solution of the sodium salt of the acid, prepared by neutralisation of the acid with sodium hydrogen carbonate, was boiled under reflux for 1 hour. No darkening took place, but again a little *p*-nitrostyrene could be isolated by steam-distillation after which most of the original acid was recovered unchanged.

(2-m-*Nitrophenylethylthio*)*acetic Acid.*—*m*-Nitrostyrene (Prausnitz, *Ber.*, 1884, **17**, 596) (3 g.) was treated with 100% mercaptoacetic acid (2 g.) and ascaridole (0·5 c.c.), and the mixture left at room

temperature for 36 hours [cf. preparation of (2-phenylethylthio)acetic acid by Kharasch, Read, and Mayo, *Chem. and Ind.*, 1938, 752]. By treatment with ether and extraction with sodium hydrogen carbonate solution, the acid was obtained as a yellow viscous oil which could neither be solidified nor distilled in a vacuum. After repeated liberation from sodium hydrogen carbonate solution and extraction with ether, it remained as an impure viscous oil (1·5 g.) (Found: N, 5·9; S, 11·1. Calc. for $C_{10}H_{11}O_4NS$: N, 5·8; S, 13·3%).

Alkaline hydrolysis. The acid was recovered as a viscous oil after being boiled with 5% aqueous sodium hydroxide for 15 minutes (Found: N, 5·1; S, 10·8%).

(2-*Phenylethylthio*)*acetic Acid.*—This acid (Holmberg, *J. pr. Chem.*, 1934, **141**, 93) was recovered completely unchanged after 0·5 hour's boiling with 5% alkali solution.

The authors express their gratitude to Professor J. Kenyon, F.R.S., for advice.

FAROUK I UNIVERSITY, FACULTY OF SCIENCE,
ALEXANDRIA.

[*Received, January 22nd,* 1951.]

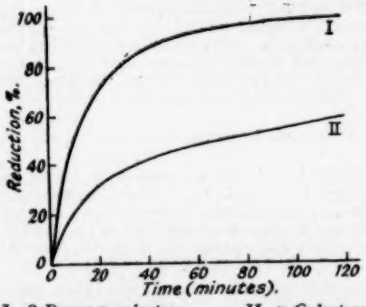
---

457. *Deoxy-sugars. Part XXII.* Comparative Rates of Oxidation and Reduction of* D-*Galactose and 2-Deoxy-*D-*galactose.*

By W. G. OVEREND, F. SHAFIZADEH, and M. STACEY.

The comparative rates of oxidation and reduction of D-galactose and its 2-deoxy-derivative have been measured. In both cases, reaction is faster with the deoxy-sugar. The results obtained are discussed with reference to other reactions of deoxy-sugars, already reported.

DURING investigations in progress in this laboratory on the polarographic behaviour of nucleic acids, it became necessary to have information concerning the relative ease of reduction of 2-deoxy-sugars compared with their normal analogues. Apart from the reduction of 2-deoxy-D-glucose with sodium amalgam to yield 2-deoxy-D-sorbitol (-mannitol) (Bergmann *et al.*, *Ber.*, 1923, **56**, 1052) little is known about the reduction of 2-deoxy-hexoses and -pentoses. We now report experiments carried out with D-galactose and 2-deoxy-D-galactose. 2-Deoxy-D-galactose was preferred in these model experiments for reasons already stated (Foster, Overend, and Stacey, *J.*, 1951, 974).



I, 2-*Deoxy*-D-*galactose.* II, D-*Galactose.*

Preliminary experiments showed that 2-deoxy-D-galactose could readily be hydrogenated catalytically to crystalline 2-deoxy-D-dulcitol, in good yield. For the study envisaged Raney nickel proved to be more suitable than platinum oxide as the catalyst. 2-Deoxy-D-dulcitol readily gave a di*iso*propylidene derivative when treated with zinc chloride in dry acetone.

Aqueous solutions of D-galactose and 2-deoxy-D-galactose, which had been allowed to mutarotate to equilibrium, were hydrogenated under identical conditions with a Raney nickel catalyst. It was readily apparent that 2-deoxy-D-galactose absorbed hydrogen faster than did D-galactose. At noted time intervals, aliquots were withdrawn from the solutions without interruption of the experiments. The amount of free reducing sugar remaining in each hydrogenation vessel was estimated from optical rotation measurements and by titration with the Shaffer–Hartmann reagent (*J. Biol. Chem.*, 1921, **45**, 377). Reasonable correlation was obtained between the two methods but the determinations by the latter method are the more accurate, and the figure shows results obtained in this way. It is clear that the deoxy-sugar is more rapidly reduced than the normal sugar.

Attempts to make corresponding measurements on the rates of oxidation of D-galactose and 2-deoxy-D-galactose by bromine are also reported. These measurements were not entirely satisfactory since although 2-deoxy-D-galactose gives the lactone, the results obtained with

* Part XXI, *J.*, 1951, 1487.

D-galactose indicated that some free galactonic acid was formed in addition to galactonolactone. However, again it appeared that reaction with the deoxy-sugar was faster than with the normal sugar.

The effect of a deoxy-group located at position 2 in pentoses and hexoses on the lability of substituents at position 1 has already been demonstrated (Overend and Stacey, *J. Soc. Food Agr.*, 1950, **1**, 168). Thus the *O*- and *N*-glycosides of 2-deoxy-sugars are more rapidly hydrolysed by acids than are the corresponding normal sugar analogues (Butler, Laland, Overend, and Stacey, *J.*, 1950, 1433). Similarly 2-deoxy-D-ribose-1 phosphate shows very great lability towards various reagents (Friedkin and Kalckar, *J. Biol. Chem.*, 1950, **184**, 449). In addition it has been shown that 2-deoxy-sugars tend to exist in the *aldehydo*-form to a greater extent than the corresponding normal hexoses and pentoses (Overend, *J.*, 1950, 2769). The oxidation and reduction results herein described further demonstrate the greater reactivity of 2-deoxy-sugars.

Experimental.

2-Deoxy-D-dulcitol.—2-Deoxy-D-galactose (1·2 g.) in solution in methanol (40 c.c.) was shaken in an atmosphere of hydrogen at a slight overpressure, at room temperature, with Raney nickel. When the absorption of hydrogen was complete, the solution was filtered and the filtrate evaporated to dryness The syrupy residue crystallised slowly and was recrystallised from methanol. *2-Deoxy-D-dulcitol* (0·7 g.) was obtained as colourless cubes, m. p. 112—113°, $[\alpha]_D^{21}$ +12° (*c*, 1·68 in methanol), +18° (*c*, 1·16 in water) (Found: C, 43·5; H, 8·4. $C_6H_{14}O_5$ requires C, 43·3; H, 8·4%).

The deoxydulcitol (0·45 g.) and zinc chloride (1·5 g.) in dry acetone (10 c.c.) were set aside for 3 days. Excess of potassium carbonate solution was then added and the mixture was filtered. Acetone was removed from the filtrate under diminished pressure and the aqueous residue was extracted with ether (4 × 50 c.c.). The solvent was removed from the extract and the syrupy residue was distilled. *Di-isopropylidene 2-deoxy-D-dulcitol* (0·23 g.) was obtained as a colourless oil, b. p. 128—130° (bath-temp.)/0·04 mm., n_D^{21} 1·4575 (Found: C, 57·9; H, 9·1. $C_{12}H_{22}O_5$ requires C, 58·5; H, 8·9%).

Measurements of Comparative Rates of Reduction of D-Galactose and 2-Deoxy-D-galactose.—(*a*) In a preliminary experiment equimolecular amounts (0·002 mol.) of D-galactose (0·36 g.) and 2-deoxy-D-galactose (0·328 g.) were separately dissolved in water (10 c.c.), and Raney nickel (0·08 g.) was added to each. The solutions were shaken under identical conditions in an atmosphere of hydrogen and at intervals the volumes of hydrogen consumed were noted. Results obtained were:

2-Deoxy-D-galactose.								
Time (minutes)	10	21	30	42	59	79	128	148
Hydrogen consumed (c.c.) ...	8	17	24	31	38	43	49	50
D-Galactose.								
Times (minutes)	11	20	41	68	80	100	115	131
Hydrogen consumed (c.c.) ...	5	9	12	15	18	20	22	23

(*b*) Equimolecular aqueous solutions (0·003 mol.) of D-galactose (0·54 g.) and 2-deoxy-D-galactose (0·492 g.), which had been allowed to mutarotate to equilibrium, were separately placed in flasks with a side-arm attached, through which samples could be conveniently withdrawn without interrupting the course of the experiment. Equal quantities of Raney nickel were added to each flask and the solutions were shaken under identical conditions in an atmosphere of hydrogen, which was led from a common reservoir to the hydrogenation vessels *via* a T-tube. At noted intervals of time, aliquots (1 c.c.) were withdrawn from both flasks. Each sample was diluted with water (to 6 c.c.) and filtered. The optical rotation of the sample was measured and then the amount of reducing groups present was estimated by use of the Shaffer–Hartmann reagent (*J. Biol. Chem.*, 1921, **45**, 377). Results obtained were as follows:

2-Deoxy-D-galactose.							
Time of hydrogenation (minutes) ...	0	5	15	30	47	85	190
$[\alpha]_D^{17}$ of solution	+57°	+50°	+30°	+25°	+20°	+15°	+15°
Calc. from				Deoxyhexose, %.			
Change in $[\alpha]_D$	100	83	36	24	12	0	0
Shaffer–Hartmann estimation	100	78	36	20	10	0	0
D-Galactose.							
Time of hydrogenation (minutes) ...	0	5	15	30	47	85	190
$[\alpha]_D^{17}$ of the solution	+81°	+71°	+62°	+57°	+53°	+40°	+18°
Calc. from				Hexose, %.			
Change in $[\alpha]_D$	100	88	76	70	64	48	22
Shaffer–Hartmann estimation	100	83	74	64	60	47	16

2-Deoxy-D-galactonolactone.—2-Deoxy-D-galactose (2·59 g.) was dissolved in water (25 c.c.), and bromine (5 c.c.) was added. The mixture was kept at 37° for 1 day or at room temperature for 1 week. After these periods the solution no longer reduced Fehling's solution. The excess of bromine was removed by aeration and the hydrogen bromide by precipitation with silver carbonate. Silver in solution was removed by treatment with hydrogen sulphide. After filtration through a charcoal pad

the filtrate was evaporated to dryness and the residue triturated with absolute methanol. Crystallisation from dry acetone gave crystals of 2-deoxy-D-galactonolactone (1·8 g.), m. p. 97—98°, $[\alpha]_D$ —33° (*c*, 1·16 in water) (Found: C, 44·4; H, 6·3. Calc. for $C_6H_{10}O_5$: C, 44·4; H, 6·2%) (cf. Overend, Shafizadeh, and Stacey, *loc. cit.*). It was shown that 2-deoxy-D-galactonolactone induced no change in the methyl-orange indicator used in the subsequent experiment.

Comparative Rates of Oxidation of D-*Galactose and 2-Deoxy-*D-*galactose.*—Bromine (1 c.c.) was added separately to equimolecular solutions (15 c.c.) of D-galactose (0·003 mol.) and 2-deoxy-D-galactose (0·003 mol.). The mixtures were kept at 15° and at intervals aliquots (1 c.c.) were withdrawn and added to distilled water (5 c.c.). Excess of bromine was removed by aeration and then the optical rotation of the sample was measured. A portion was titrated with 0·02N-potassium carbonate, with methyl-orange as indicator. Results were as follows:

*2-Deoxy-*D-*galactose.*					
Time (hours)	0	4·75	6·5	9	24
Calc. from			Deoxyhexose, %.		
$[\alpha]_D$ measurements	100	24	7	3	3
Titration	100	24	6	0	0
D-*Galactose.*					
Time (hours)	0	4·75	6·5	9	24
Calc. from			Hexose, %.		
$[\alpha]_D$ measurements	100	63	40	27	3
Titration	100	42	28	18	<2

(Cf. Kiliani, *Ber.*, 1922, **55**, 75; Pryde, *J.*, 1923, 1808.)

The authors thank the British Empire Cancer Campaign for financial assistance, and one of them (F. S.) is grateful for a personal grant.

THE CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM, 15.

[*Received, March 22nd*, 1951.]

---

458. *The Synthesis and Reactions of Branched-chain Hydrocarbons. Part I. Hydrocarbons with the 3 : 5 : 5-Trimethylhexyl Group.*

By E. M. GUTMAN and W. J. HICKINBOTTOM.

The preparation of 2 : 2 : 4 : 7 : 10 : 12 : 12-heptamethyltridecan-7-ol and of 2 : 2 : 4 : 10 : 12 : 12-hexamethyl-7-(3 : 5 : 5-trimethylhexyl)tridecan-7-ol is described. By successive dehydration and hydrogenation 2 : 2 : 4 : 7 : 10 : 12 : 12-heptamethyltridecane and 2 : 2 : 4 : 10 : 12 : 12-hexamethyl-7-(3 : 5 : 5-trimethylhexyl)tridecane are obtained. Ozonolysis of the olefins is described. 2 : 2 : 4 : 9 : 11 : 11-Hexamethyldodecane is prepared by the action of silver bromide on the Grignard compound from 1-chloro-3 : 5 : 5-trimethylhexane.

THIS paper is the first of a series which has for its object the study of the reactions and properties of paraffins with a regular pattern of quaternary carbon atoms. A necessary preliminary is the development and exploitation of methods for the unambiguous synthesis of hydrocarbons of suitable structure.

The method which so far has been most useful for the direct synthesis of hydrocarbons with a quaternary carbon atom consists in the reaction of an alkyl halide with a suitable metal alkyl. Zinc alkyls have been used successfully for this purpose (Friedel and Ladenburg, *Annalen*, 1867, **142**, 310; Goriainow, *ibid.*, 1873, **165**, 107; Markownikoff, *Ber.*, 1899, **32**, 1445; 1900, **33**, 1905; Noller, *J. Amer. Chem. Soc.*, 1929, **51**, 594). Their value for the present work is seriously impaired by partial isomerisation which occurs during the reaction if highly branched compounds are used (Buck, Elsner, *et al.*, *J. Inst. Petr.*, 1948, **34**, 339). The risk of isomerisation is reduced if alkylmagnesium halides are used instead of zinc alkyls, but their use is attended by the inconvenience of low yields and of the presence of a considerable proportion of other products.

One suitable line of approach is to use in usual synthetic reactions alkylmagnesium halides having quaternary carbon atoms. It is one of the primary objects of this work to explore the possibilities and limitations of such compounds.

1-Chloro-3 : 5 : 5-trimethylhexane seemed a suitable compound for this purpose, in that it can be prepared in good yield from the readily accessible 3 : 5 : 5-trimethylhexan-1-ol. It appears from qualitative observations that the chloride is not very reactive; for its hydrolysis, prolonged boiling with aqueous alkali is necessary; potassium cyanide yields the corresponding nitrile slowly and only after long boiling. It reacts sluggishly in ether with magnesium to form the corresponding Grignard compound. Under suitable conditions a yield of about 80% of the alkylmagnesium chloride is obtained and the solution so formed reacts smoothly and normally with esters of carboxylic acids to give tertiary alcohols. The present paper describes the preparation of 2 : 2 : 4 : 7 : 10 : 12 : 12-heptamethyltridecan-7-ol (I) and 2 : 2 : 4 : 10 : 12 : 12-hexamethyl-7-(3 : 5 : 5-trimethylhexyl)tridecan-7-ol (IV). These alcohols are dehydrated to the olefins (II) and (III) from the first and (V) from the second without change of structure by heating them with a small amount of iodine.

$(CMe_3\cdot CH_2\cdot CHMe\cdot CH_2\cdot CH_2)_2CMe\cdot OH$ (I.)

$CMe_3\cdot CH_2\cdot CHMe\cdot CH_2\cdot CH{:}CMe\cdot CH_2\cdot CH_2\cdot CHMe\cdot CH_2\cdot CMe_3$ (II.)

$(CMe_3\cdot CH_2\cdot CHMe\cdot CH_2\cdot CH_2)_2C{:}CH_2$ (III.)

$(CMe_3\cdot CH_2\cdot CHMe\cdot CH_2\cdot CH_2)_2C\cdot OH$ (IV.)

$(CMe_3\cdot CH_2\cdot CHMe\cdot CH_2\cdot CH_2)_2C{:}CH\cdot CH_2\cdot CHMe\cdot CH_2\cdot CMe_3$ (V.)

$(CMe_3\cdot CH_2\cdot CHMe\cdot CH_2\cdot CH_2)_3$ (VI.)

The structure of these olefins was established by ozonolysis and comparison of the products so obtained with synthetic specimens.

The Grignard compound from 1-chloro-3 : 5 : 5-trimethylhexane reacts with dry silver bromide to give 2 : 2 : 4 : 9 : 11 : 11-hexamethyldodecane (VI); in this reaction a notable proportion of an olefin was also formed.

Experimental.

(Analyses by Drs. Weiler and Strauss.)

Preparation of 1-*Chloro*-3 : 5 : 5-*trimethylhexane*.—3 : 5 : 5-Trimethylhexan-1-ol, a gift from Imperial Chemicals Industries Limited, Billingham, had the following constants: b. p. 85°/11 mm., n_D^{20} 1·4330; it was characterised by its 3 : 5-dinitrobenzoate, m. p. 63°, and its 3-nitrophthalic hydrogen ester, m. p. 150°.

The alcohol (144 g.), diluted with dry pyridine (79 g.), was cooled in ice and mechanically stirred while redistilled thionyl chloride (125 g.) was added gradually. An exothermic reaction developed and a bulky solid separated. When the addition had been completed, stirring was continued for a further 20 minutes. The reaction mixture was then gradually heated to 110° and kept at this temperature till the evolution of sulphur dioxide had ceased (2—4 hours). The product was isolated by pouring the mixture into water and washing the organic layer successively with water, dilute sulphuric acid, aqueous sodium carbonate, and water. The dried liquid on fractionation through an efficient column gave pure 1-*chloro*-3 : 5 : 5-*trimethylhexane*, b. p. 70°/17 mm., n_D^{25} 1·4332 (yield 147 g., 91%) (Found: C, 66·4; H, 11·5; Cl, 21·9, 22·0. $C_9H_{19}Cl$ requires C, 66·4; H, 11·8; Cl, 21·8%). Bruner (*Ind. Eng. Chem.*, 1949, **41**, 2861) gives b. p. 179—180°/760 mm., n_D^{25} 1·4304, for this chloride prepared by the action of hydrogen chloride on the alcohol at 135°, but does not give an analysis.

The chloride is hydrolysed very slowly by aqueous alkali; it reacts only sluggishly in ether with magnesium. From 0·2 g.-mol. of chloride, the corresponding Grignard compound was prepared in 78% yield, after the reaction had been started by the addition of 4 drops of methyl iodide. Oxidation of the Grignard compound in ether by molecular oxygen gave 3 : 5 : 5-trimethylhexan-1-ol, b. p. 80—85°/12 mm., $n_D^{20\cdot5}$ 1·4329—1·4332 (67% calculated on the chloride used); its 3 : 5-dinitrobenzoate had m. p. and mixed m. p. 63°. 1-*Bromo*-3 : 5 : 5-*trimethylhexane*, b. p. 75°/12 mm., n_D^{20} 1·4527, was isolated in 70% yield by refluxing the alcohol (19·8 g.) with hydrobromic acid (48%, 60 g.) and concentrated sulphuric acid (15·5 g.) for 6 hours (Found: C, 52·8; H, 9·2; Br, 38·2. $C_9H_{19}Br$ requires C, 52·2; H, 9·2; Br, 38·6%) (Bruner, *loc. cit.*, gives b. p. 70—71°/11 mm., n_D^{25} 1·4510, for the bromide prepared by the action of hydrogen bromide at 150°, but gives no analysis).

Preparation of 2 : 2 : 4 : 7 : 10 : 12 : 12-*Heptamethyltridecane*.—The Grignard reagent [from 1-chloro-3 : 5 : 5-trimethylhexane (65 g., 0·4 mol.), magnesium (9·8 g.), and ether (150 ml.)] was added to ethyl acetate (14·4 g., 0·16 mol.), and the reaction completed by heating the mixture under reflux. The product was decomposed by ice and ammonium chloride, and the washed ethereal solution fractionally distilled. 2 : 2 : 4 : 7 : 10 : 12 : 12-*heptamethyltridecan*-7-*ol* (I) was collected at 124—126°/0·9 mm.; the yield was 38 g. (78%). The pure alcohol is a colourless viscous oil, b. p. 120°/0·5 mm., n_D^{20} 1·4512 (Found: C, 80·5; H, 13·7. $C_{20}H_{42}O$ requires C, 80·5; H, 14·1%).

Dehydration was effected by heating the alcohol (28 g.) with a few crystals of iodine in a flask fitted with a reflux condenser and a partial take-off head, till no more water was collected (1·1 ml.) (½ hour). The residue, after being washed with water and thiosulphate solution, was dried and refluxed over sodium for 3 hours. It distilled at 101—103°/0·55 mm., n_D^{20} 1·4389—1·4398, and consisted largely of 2 : 2 : 4 : 7 : 10 : 12 : 12-*heptamethyltridec*-6-*ene* (II) with a small proportion of 5 : 7 : 7-trimethyl-2-(3 : 5 : 5-trimethylhexyl)oct-1-ene (III) (Found: C, 85·8; H, 14·1. $C_{20}H_{40}$ requires C, 85·6; H, 14·4%).

Ozonolysis of the olefin (22 g.) in chloroform gave formaldehyde (dimedone derivative, m. p. and mixed m. p. 189°) and 5 : 7 : 7-trimethyloctan-2-one (b. p. 92—101°/32 mm., 8·5 g.; n_D^{20} 1·4284—1·4292), which formed a 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 79°. Systematic fractionation of the higher-boiling fractions of the neutral product of ozonolysis gave a further amount of the above ketone (1·8 g.) and a small fraction (0·6 g.), b. p. 120—134°/1·3 mm., having characteristics similar to those of 2 : 2 : 4 : 10 : 12 : 12-hexamethyltridecan-7-one although no crystalline derivatives could be prepared from it. The acidic product of the ozonolysis boiled at 126—129°/15 mm. (4·6 g.), $n_D^{20\cdot1}$ 1·4297, and was identified as 2 : 4 : 4-trimethylpentane-1-carboxylic acid by its physical constants (the pure acid given by Imperial Chemical Industries Limited, Billingham, had b. p. 125°/12 mm., $n_D^{20\cdot1}$ 1·4295) and its *S*-*benzylthiuronium* salt, m. p. and mixed m. p. 154° (Found : C, 63·2; H, 8·6; N, 8·4. $C_{17}H_{28}O_2N_2S$ requires C, 62·9; H, 8·6; N, 8·6%).

Hydrogenation of the olefin (20 g.) in ethyl alcohol (Raney nickel at 150°/39 atm.) gave 2 : 2 : 4 : 7 : 10 : 12 : 12-*heptamethyltridecane*. It was purified from traces of olefin by percolating the distilled hydrocarbon through a column of silica gel followed by a further fractionation and had b. p. 112°/0·5 mm. (16 g., 79%), n_D^{20} 1·4437, d_{15}^{15} 0·7901 (Found : C, 85·0; H, 14·65. $C_{20}H_{42}$ requires C, 85·0; H, 15·0%).

5 : 7 : 7-*Trimethyloctan*-2-*one*.—For purposes of comparison this ketone was prepared, but not in very good yield, by two methods.

(i) 1-Cyano-3 : 5 : 5-trimethylhexane (5·3 g.) in ether (15 ml.) was added slowly to a solution prepared from methyl iodide (5·85 g.), magnesium (1 g.), and ether (15 ml.). A gentle reaction occurred and it was completed by heating the solution under reflux for 1 hour. Decomposition of the product with aqueous acid and fractionation gave 5 : 7 : 7-trimethyloctan-2-one (1·6 g.), b. p. 103°/28 mm., n_D^{20} 1·4309, and unidentified higher-boiling material (2·4 g.).

(ii) The filtered Grignard reagent from 1-chloro-3 : 5 : 5-trimethylhexane (19·5 g.) and magnesium (2·95 g.) in ether was stirred and refluxed with finely powdered cadmium chloride (12·8 g.) for 3 hours. The ether was removed next morning and replaced by benzene (70 ml.). A solution of acetyl chloride (7·6 g.) in dry benzene (20 ml.) was added slowly, and the mixture stirred and heated. After 3 hours the orange-coloured, viscous reaction product was decomposed by aqueous sulphuric acid, and the benzene layer fractionally distilled to give crude 5 : 7 : 7-trimethyloctan-2-one (6·1 g.), b. p. 94—100°/22 mm., n_D^{20} 1·4346—1·4359.

The pure *ketone*, b. p. 103°/28 mm., n_D^{20} 1·4309 (Found : C, 78·0; H, 13·0. $C_{11}H_{22}O$ requires C, 77·6; H, 13·0%), was purified through its semicarbazone, m. p. 147·5—148·5°, and 2 : 4-*dinitrophenylhydrazone*, m. p. 80° (Found : C, 58·6; H, 7·2; N, 15·5. $C_{17}H_{26}O_4N_4$ requires C, 58·3; H, 7·4; N, 16·0%).

3 : 3 : 5-*Trimethylhexane*-1-*carboxylic Acid*.—A solution of potassium cyanide (78 g.) in water (75 ml.) and alcohol (170 ml.) was refluxed with 1-chloro-3 : 5 : 5-trimethylhexane (97·5 g.) for 72 hours. Fractionation of the water-insoluble product gave the required *nitrile* (59·5 g.), b. p. 97—98°/11 mm., $n_D^{20\cdot7}$ 1·4294 (Found : C, 78·1; H, 12·55; N, 9·1. $C_{10}H_{19}N$ requires C, 78·4; H, 12·5; N, 9·1%). Hydrolysis of the nitrile (20 g.) with hot aqueous-alcoholic sodium hydroxide for 24 hours gave, after acidification, 3 : 3 : 5-*trimethylhexane*-1-*carboxylic acid* (19·8 g.), b. p. 132—133°/8 mm., $n_D^{21\cdot2}$ 1·4346 (Found : C, 69·6; H, 11·6. $C_{10}H_{20}O_2$ requires C, 69·7; H, 11·7%). Its *S*-*benzylthiuronium* salt had m. p. 155° (Found : N, 8·2; S, 9·0. $C_{18}H_{32}O_2N_2S$ requires N, 8·2; S, 9·4%); the chloride had b. p. 104°/22 mm., n_D^{20} 1·4411; the *amide* m. p. 107° (Found : C, 70·1; H, 12·3; N, 8·3. $C_{10}H_{21}ON$ requires C, 70·0; H, 12·3; N, 8·2%); and the *ethyl* ester b. p. 96·5°/9 mm., $n_D^{21\cdot3}$ 1·4254 (Found : C, 72·4; H, 11·75. $C_{12}H_{24}O_2$ requires C, 72·0; H, 12·0%).

2 : 2 : 4 : 10 : 12 : 12-*Hexamethyl*-7-(3 : 5 : 5-*trimethylhexyl*)*tridecane*.—The foregoing ethyl ester (40 g.) in ether (60 ml.) was added dropwise to a Grignard reagent prepared from 1-chloro-3 : 5 : 5-trimethylhexane (80·5 g.), magnesium (12·15 g.), and dry ether (150 ml.). The reaction was completed by warming the mixture under reflux for 1 hour, and the product was then decomposed with ice and ammonium chloride acidified with hydrochloric acid. Distillation gave some unchanged chloride, some 3 : 5 : 5-trimethylhexan-1-ol, and a main fraction consisting of 2 : 2 : 4 : 10 : 12 : 12-*hexamethyl*-7-(3 : 5 : 5-*trimethylhexyl*)*tridecan*-7-*ol* (IV), b. p. 176—178°/0·8 mm., n_D^{20} 1·4558—1·4559 (60 g.) (Found : C, 82·0; H, 13·8. $C_{33}H_{68}O$ requres C, 81·9; H, 14·2%), a viscous oil.

Dehydration was effected by heating the alcohol (40 g.) with a few crystals of iodine at 200° for 3 hours, although it seemed from the amount of water evolved that the reaction was substantially complete within 15 minutes. The olefin, 2 : 2 : 4 : 10 : 12 : 12-*hexamethyl*-7-(3 : 5 : 5-*trimethylhexyl*)-*tridec*-7-*ene*, after being washed with thiosulphate solution and refluxed over sodium, distilled at 161—162°/0·8 mm. as a colourless viscous liquid (31 g.), $n_D^{20\cdot4}$ 1·4548—1·4549 (Found : C, 85·6; H, 14·2. $C_{33}H_{66}$ requires C, 85·6; H, 14·4%).

Ozonolysis of the olefin (8·6 g.) in chloroform gave 2 : 2 : 4 : 10 : 12 : 12-hexamethyltridecan-7-one (1·9 g.), b. p. 124—127°/0·8 mm., characterised by its semicarbazone, m. p. and mixed m. p. 69°, and 2 : 4 : 4-trimethylpentane-1-carboxylic acid (2·8 g.), b. p. 128—131°/16 mm., $n_D^{20\cdot3}$ 1·4292, which gave an *S*-benzylthiuronium salt, m. p. and mixed m. p. 154°.

Hydrogenation of the olefin (30·5 g.) in ethyl alcohol (150 ml.) (Raney nickel at 180°/27 atm.) gave 2 : 2 : 4 : 10 : 12 : 12-*hexamethyl*-7-(3 : 5 : 5-*trimethylhexyl*)*tridecane*. This was freed from traces of unchanged olefin by passing its solution in heptane (15 ml.) through a column filled with silica gel and subsequent fractionation; the pure hydrocarbon (24·1 g., 78%) had b. p. 166°/0·5 mm., n_D^{20} 1·4558, d_{20}^{20} 0·8152 (Found : C, 85·3; H, 14·8. $C_{33}H_{68}$ requires C, 85·2; H, 14·8%).

2 : 2 : 4 : 10 : 12 : 12-*Hexamethyltridecan*-7-*one* was prepared in 68% yield by reaction of the chloride from 3 : 5 : 5-trimethylhexanecarboxylic acid (20·5 g.) with di-(3 : 5 : 5-trimethylhexyl)cadmium [from

the Grignard reagent from 1-chloro-3 : 5 : 5-trimethylhexane (31 g.) in benzene]. It had b. p. 124°/1·1 mm., n_D^{20} 1·4460 (Found : C, 81·2; H, 13·4. $C_{19}H_{38}O$ requires C, 80·8; H, 13·5%); *semicarbazone*, m. p. 69° (Found : N, 12·3. $C_{20}H_{41}ON_3$ requires N, 12·4%); its 2 : 4-dinitrophenylhydrazone had m. p. 39°.

2 : 2 : 4 : 9 : 11 : 11-*Hexamethyldodecane*.—To the filtered and cooled Grignard reagent from 1-chloro-3 : 5 : 5-trimethylhexane (32·5 g.) was added dry silver bromide (37·6 g.) (Gardner and Bergstrom, *J. Amer. Chem. Soc.*, 1929, **51**, 3375). The solution became black and silver was precipitated. Efficient stirring was maintained throughout the addition and for 1 hour after all the silver bromide had been added. The reaction was completed by heating under reflux for 1 hour. Distillation after removal of inorganic material gave low-boiling material (7·5 g.), b. p. 39—70°/11 mm., and 2 : 2 : 4 : 9 : 11 : 11-*hexamethyldodecane*, b. p. 136°/8 mm. (8·2 g.). Traces of olefin were removed by shaking it with small amounts of concentrated sulphuric acid, and the purification completed by refluxing over sodium; b. p. 138·5°/10 mm., n_D^{20} 1·4370 (Found : C, 84·7; H, 15·05. $C_{18}H_{38}$ requires C, 84·95; H, 15·05%).

The work described in this paper is part of a programme sponsored and financed by the Institute of Petroleum. The authors are also indebted to Imperial Chemical Industries Limited, Billingham, for a generous gift of 3 : 5 : 5-trimethylhexan-1-ol and for a sample of 2 : 4 : 4-trimethylpentane-1-carboxylic acid, and to Professor F. H. Garner, O.B.E., for kindly placing the facilities of his department at their disposal to allow the hydrogenation of the olefins to be carried out.

QUEEN MARY COLLEGE, LONDON, E.1. [*Received, March 27th*, 1951.]

---

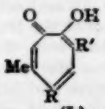
459. *Purpurogallin. Part VIII.* Nitration and Nitrosation of β-Methyltropolone.*

By ROBERT D. HAWORTH and PHILLIP R. JEFFERIES.

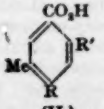
Nitrosation of β-methyltropolone gives a γ-nitroso-derivative, and nitration yields a mixture of γ-, α-, and α′-nitro-compounds, with the first predominating. The structure of the nitro-compounds has been established by rearrangement in the presence of alkalis to nitro-*m*-toluic acids. Reduction to the γ-, α-, and α′-amines has been examined, and the γ-amine was identical with the amine obtained (see Part IV) by reduction of *p*-tolylazo-β-methyltropolone, thus proving that diazo-coupling occurs in the γ-position in β-methyltropolone. The α- and α′-amino-tropolones gave diazo-compounds, but when warmed with dilute sulphuric acid the solutions of these compounds, instead of yielding the α- and α′-hydroxytropolones, underwent ring contraction and rearrangement and gave 6- and 4-methylsalicylic acid, respectively. The mechanism of the rearrangement is discussed.

IN a recent paper, Doering and Knox (*J. Amer. Chem. Soc.*, 1951, **73**, 828) describe the preparation of a nitro- and a nitroso-tropolone, and we now record some of our results concerning substitution in β-methyltropolone. A preliminary report on some of this work has been described elsewhere (*Chem. and Ind.*, 1950, 841).

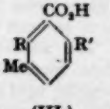
We have examined nitration and nitrosation of β-methyltropolone (I; R = R′ = H), and although oxidation played a prominent rôle, by nitration in acetic acid at 0°, molar quantities of nitric acid being used, we were able to isolate three mononitro-β-methyltropolones, m. p. 176—177°, 146—147°, and 206°, severally, together with a small quantity of a carboxylic acid, m. p. 172—173°, which was found to be 4 : 6-dinitro-*m*-toluic acid (II; R = R′ = NO_2) by comparison with a sample prepared from 4 : 6-dinitro-*m*-xylene (Errera and Maltese, *Gazzetta*, 1903, **33**, II, 278). The formation of (II; R = R′ = NO_2) must have been due to a benzilic



(I.)



(II.)

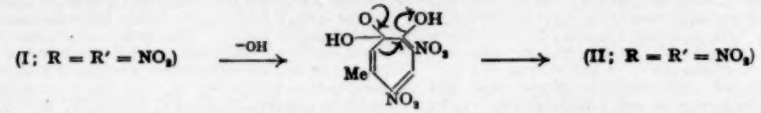


(III.)

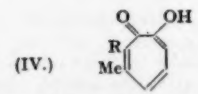
acid type rearrangement of β-methyl-α′γ-dinitrotropolone (I; R = R′ = NO_2) either during the reaction or in the process of isolation. Nozoe's observation (for references, see Part IV, *J.*, 1951,

* Part VII, *J.*, 1951, 1325.

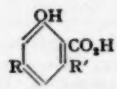
561) that dinitrohinokitiol rearranges to a dinitro*iso*propylbenzoic acid when warmed with water, and the results reported below illustrate the marked influence of nitro-substituents in accelerating the benzilic acid type changes in the tropolones; the effect is in accordance with the polar nature of the nitro-group which increases the attraction for the hydroxyl ion necessary for the transformation



The bulk (60%) of the β-methylnitrotropolone mixture consisted of β-methyl-γ-nitrotropolone (I; R = NO_2, R′ = H), m. p. 176—177°, which underwent a benzilic acid type rearrangement when warmed with 2N-sodium hydroxide. The acidic product, m. p. 214—215°, was shown to be 6-nitro-*m*-toluic acid (II; R = NO_2, R′ = H) by comparison with an authentic sample obtained by oxidation of 4-nitro-*m*-xylene (Beilstein and Kreusler, *Annalen*, 1867, **144**, 168; Muller, *Ber.*, 1909, **42**, 430). The orientation of β-methyl-α′-nitrotropolone (I; R = H, R′ = NO_2), m. p. 146—147°, obtained in 14% yield, was established similarly by conversion into 4-nitro-*m*-toluic acid, m. p. 132—133°, identified by comparison with a sample obtained by nitration of *m*-toluic acid (Finkeldee, *Ber.*, 1905, **38**, 3542; Muller, *loc. cit.*). The β-methyl-α-nitrotropolone (IV; R = NO_2), m. p. 206°, isolated in 8% yield, was more stable to alkali than the isomers, but short warming with 30% sodium hydroxide gave an excellent yield of an acid, m. p. 218—219°, identical with 2-nitro-*m*-toluic acid (III; R = NO_2, R′ = H) (Muller, *loc. cit.*).



(IV.)



(V.)

Reduction of β-methyl-γ-nitrotropolone (I; R = NO_2, R′ = H) with sodium dithionite gave γ-amino-β-methyltropolone (I; R = NH_2, R′ = H), m. p. 224° (decomp.), which yielded a benzylidene derivative, m. p. 145—146°. γ-Amino-β-methyltropolone was found to be identical with the amine prepared (Part IV, *loc. cit.*) by reductive fission of *p*-tolylazo-β-methyltropolone. Hence, diazo-coupling must have occurred in the γ-position of the tropolone nucleus, and the hydroxy-compound prepared from this amine as in Part IV must be γ-hydroxy-β-methyltropolone (I; R = OH, R′ = H). The aromatic character of the γ-amino-group is also shown by decomposition of the diazonium sulphate with potassium iodide, whereby γ-iodo-β-methyltropolone (I; R = I, R′ = H), m. p. 169—170°, was obtained.

Treatment of β-methyltropolone with nitrous acid gave β-methyl-γ-nitrosotropolone (I; R = NO, R′ = H), m. p. 178° (decomp.), the structure of which was established by reduction in the presence of a palladium catalyst, 2 moles of hydrogen being absorbed and γ-amino-β-methyltropolone (I; R = NH_2, R′ = H) obtained.

In the presence of a palladium catalyst, hydrogen readily reduced β-methyl-α′-nitrotropolone to α′-amino-β-methyltropolone (I; R = H, R′ = NH_2), m. p. 136—137°, and in the same way β-methyl-α-nitrotropolone gave α-amino-β-methyltropolone (IV; R = NH_2), m. p. 151°. Both these new amines, like the previously described γ-isomer, are yellow compounds which show characteristic tropolone ultra-violet absorption spectra (p. 2071). The α- and α′-amines react with nitrous acid very readily at 0° to give highly coloured diazonium solutions from which we had hoped to prepare the corresponding hydroxytropolones by the method described in Part IV for γ-hydroxy-β-methyltropolone. The products from α- and α′-amines, which were obtained in high yield, gave violet ferric tests reminiscent of salicylic acid, and the ultra-violet absorption spectra indicated in both cases that the compounds were benzenoid and that the tropolone ring was absent. The substance obtained from α-amino-β-methyltropolone was shown to be identical with a specimen of 6-methylsalicylic acid (V; R = H, R′ = Me) prepared from 6-methylanthranilic acid (Gabriel and Thieme, *Ber.*, 1919, **52**, 1079; Mayer and Schulze, *Ber.*, 1925, **58**, 1469), and the acid obtained from α′-amino-β-methyltropolone was shown to be 4-methylsalicylic acid (V; R = Me, R′ = H), m. p. 177° (Tiemann and Schotten, *Ber.*, 1878, **11**, 777; Duff, *J.*, 1941, 547). It is unlikely that the ring contractions occur during the reactions of nitrous acid with the α- and α′-aminotropolones because the resultant red solutions have the properties of diazonium solutions and couple with alkaline β-naphthol. It is equally improbable

that the diazo-group is replaced by hydroxyl during the reaction because α- and α′-hydroxytropolones are quite stable in the presence of hot dilute acids: for example, puberulonic acid is decarboxylated to puberulic acid by being boiled with 2N-sulphuric acid (Corbett, Hassell, Johnson, and Todd, *J.*, 1950, 4). The most probable explanation * of these ring contractions is that they occur simultaneously with the elimination of nitrogen from the diazonium salts by a mechanism which is illustrated below for the transformation in the case of α′-amino-β-methyltropolone, and a similar scheme may be advanced for the corresponding α-amine.

On the other hand, an application of this mechanism to the case of γ-amino-β-methyltropolone would require the formation of β-(2-hydroxy-4-methyl*cyclo*buta-1 : 3-dienyl)acrylic acid, and replacement of the diazonium group by hydroxyl with the production of γ-hydroxy-β-methyltropolone as described in Part IV (*loc. cit.*) would obviously meet with less resistance.

Experimental.

β-Methyltropolone was prepared from purpurogallin *via* β-carbomethoxy-α-carboxytropolone by the method described in Part IV (*loc. cit.*).

Nitration of β-Methyltropolone.—Preliminary experiments showed that the reaction was complex and accompanied by considerable oxidation, but by working in cold acetic acid solution at 0° satisfactory results were obtained. β-Methyltropolone (0·5 g.) in glacial acetic acid (2·5 ml.) was cooled in ice, and nitric acid (0·25 ml.; d_4^{20} 1·41) added with agitation. An orange colour developed, and after 30 minutes at 0° the precipitate was removed and washed with water. The material obtained from ten such runs was fractionally crystallised from alcohol to give (*a*) long prisms of *β-methyl-γ-nitrotropolone* (I; R = NO_2, R′ = H) (2·0 g.), m. p. 176—177°, which for analysis were sublimed at 130°/11 mm. (Found: C, 52·8; H, 3·9; N, 8·1. $C_8H_7O_4N$ requires C, 53·0; H, 3·9; N, 7·7%), and (*b*) prisms of *β-methyl-α-nitrotropolone* (IV; R = NO_2) (0·4 g.), m. p. 206° (Found: C, 52·5; H, 4·1; N, 7·4%). The acetic acid filtrate was diluted with water (200 ml.), and the precipitate (0·5 g.) (*A*) separated. The filtrate was extracted with chloroform (4 × 100 ml.) and washed with sodium hydrogen carbonate solution, the organic layer dried, and the solvent removed. From the tarry residue β-methyltropolone (0·6 g.) was recovered by extraction with hot light petroleum (b. p. 60—80°), but the residual amorphous residue did not yield any further crystalline material. On acidification the sodium hydrogen carbonate washings yielded a precipitate (0·4 g.) (*B*) which was removed, and the filtrate on extraction with chloroform and evaporation of the dried extract gave a residue which deposited crystals (0·2 g.) (*C*) from the minimum volume of boiling alcohol. The mother-liquor was precipitated with water, and after solidification the precipitate (0·25 g.) was removed and crystallised from benzene (charcoal); elongated plates of 4 : 6-dinitro-*m*-toluic acid, m. p. 172—173° (Found: C, 42·6; H, 3·0; N, 12·4%; equiv., 229. Calc. for $C_8H_6O_8N_2$: C, 42·5; H, 2·7; N, 12·4%; equiv., 226), were obtained and identified by comparison with an authentic sample prepared by oxidation of 4 : 6-dinitro-*m*-xylene (Errera and Maltese, *loc. cit.*). Excess of ethereal diazomethane gave the *methyl* ester, m. p. 105° (Found: C, 45·3; H, 3·7. $C_9H_8O_8N_2$ requires C, 45·0; H, 3·4%). The materials (*A*), (*B*), and (*C*) were mixtures, and fractional crystallisation from alcohol yielded yellow plates of *β-methyl-α′-nitrotropolone* (I; R = H, R′ = NO_2) (0·7 g.), m. p. 146—147° (Found: C, 53·2; H, 4·0; N, 7·7%), and a further crop of β-methyl-α-nitrotropolone (0·15 g.).

The three mononitro-β-methyltropolones gave a red-green colour with alcoholic ferric chloride and slowly dissolved in sodium hydrogen carbonate to give orange solutions.

Alkaline Rearrangement of β-Methyl-γ-nitrotropolone.—Unchanged material was recovered after boiling the nitro-compound with aqueous sodium carbonate or 2N-sulphuric acid. β-Methyl-γ-nitrotropolone (0·2 g.) was refluxed with 2N-sodium hydroxide (3 ml.) for 1 hour. The dark solution was acidified with 2N-sulphuric acid, and the suspension extracted with ether (3 × 20 ml.). Evaporation of the dried extract gave an amorphous residue which was purified by sublimation at 120°/8 mm. Crystallisation from 50% aqueous alcohol gave long prisms of 6-nitro-*m*-toluic acid (0·05 g.), m. p. 214—215° (Found: equiv., 175. Calc. for $C_8H_7O_4N$: equiv., 181), alone or mixed with an authentic sample prepared by oxidation of 4-nitro-*m*-xylene (Beilstein and Kreusler, *loc. cit.*; Muller, *loc. cit.*). Comparison of samples of the methyl ester, m. p. 81—82° (Herre, *Ber.*, 1895, **28**, 597), confirmed the identity.

Alkaline Rearrangement of β-Methyl-α′-nitrotropolone.—The nitro-compound (0·2 g.) was heated under reflux with 2N-sodium hydroxide (3 ml.) for 30 minutes. The cooled dark solution was acidified with 2N-sulphuric acid, the suspension extracted with ether (3 × 25 ml.) which was washed with sodium

* When this manuscript was completed a brief statement of some recent observations by Nozoe and his co-workers came to hand (*J. Amer. Chem. Soc.*, 1951, **73**, 1895). The conversion of α- and α′-aminohinokitiol into 6- and 4-*iso*propylsalicylic acids, respectively, is described, and a mechanism similar to that proposed above is suggested.

hydrogen carbonate solution, and the acidic material recovered, isolated with ether, and sublimed at 130°/10 mm. The colourless sublimate (0·041 g.) was crystallised first from benzene, then from water, to give needles of 4-nitro-*m*-toluic acid, m. p. 132—133°, alone or mixed with an authentic sample obtained by nitration of *m*-toluic acid (Muller, *loc. cit.*; Finkeldee, *loc. cit.*). The methyl ester, prepared with an excess of ethereal diazomethane, had m. p. 78—79°, alone or mixed with methyl 4-nitro-*m*-toluate (Jurgens, *Ber.*, 1907, **40**, 4411).

Alkaline Rearrangement of β-Methyl-α-nitrotropolone.—This substance was scarcely affected by the above treatment with 2N-sodium hydroxide, and alkali fusion at 140—150° produced only amorphous material. The nitrotropolone (0·3 g.) was refluxed with 30% sodium hydroxide solution for 10 minutes. Acidification of the cooled solution gave a clean precipitate which was extracted with ether and recovered by washing it with sodium hydrogen carbonate and acidification. The product (0·22 g.) after two crystallisations from 50% aqueous alcohol yielded 2-nitro-*m*-toluic acid, m. p. 218—219° (Found: equiv., 179. Calc. for $C_8H_7O_4N$: equiv., 181), undepressed by admixture with an authentic sample, m. p. 219—220°, obtained by nitration of *m*-toluic acid (Muller, *loc. cit.*). The methyl ester, prepared with an excess of ethereal diazomethane, had m. p. 72—73°, alone or mixed with a sample of methyl 2-nitro-*m*-toluate (Muller, *loc. cit.*).

γ-Amino-β-methyltropolone (I; R = NH_2, R′ = H).—β-Methyl-γ-nitrotropolone (0·2 g.) was suspended in water (10 ml.) and treated with 10% aqueous sodium dithionite (10 ml.) containing 2N-sodium hydroxide (1 ml.). The colour of the solution changed fairly quickly from orange to light yellow. The solution was acidified with dilute hydrochloric acid, made slightly alkaline with ammonia solution, and acidified with a little acetic acid. Repeated extraction with ethyl methyl ketone gave, on distillation of the dried extract, a yellow residue (0·18 g.), which was sublimed at 190°/0·5 mm. Crystallisation from alcohol gave yellow prisms of γ-amino-β-methyltropolone, m. p. 224° (decomp.) (Found: C, 63·2; H, 6·0; N, 9·4. Calc. for $C_8H_9O_2N$: C, 63·5; H, 6·0; N, 9·3%), alone or mixed with a sample of amine prepared from *p*-tolylazo-β-methyltropolone by the method described in Part IV (*loc. cit.*). The identity was confirmed by the preparation, in alcoholic solution, of a *benzylidene* derivative, m. p. 145—146° (Found: C, 74·9; H, 5·5; N, 6·0. $C_{15}H_{13}O_2N$ requires C, 75·3; H, 5·5; N, 5·9%), which gives a purple ferric test.

γ-Iodo-β-methyltropolone (I; R = I, R′ = H).—The above amino-compound (0·27 g.) in water (5 ml.) and sulphuric acid (0·4 ml.) was cooled to 10° and diazotised by gradual addition of sodium nitrite (0·13 g.) in water (2 ml.), an orange solution being obtained. Decomposition was brought about by addition to potassium iodide (2 g.) in water (5 ml.) and gentle heating, followed by 5 minutes' boiling. The cooled suspension was extracted with ether, and the extract washed with sodium thiosulphate solution, dried, and evaporated. Repeated extraction of the residue with *cyclo*hexane gave *γ-iodo-β-methyltropolone*, which separated from acetone in cream plates (0·219 g.), m. p. 169—170° (Found: C, 37·1; H, 2·7; I, 48·2. $C_8H_7O_2I$ requires C, 36·7; H, 2·5; I, 48·5%); it gives a green colour with alcoholic ferric chloride.

β-Methyl-γ-nitrosotropolone (I; R = NO, R′ = H).—β-Methyltropolone (0·5 g.) was dissolved in acetic acid (5 ml.), and water (10 ml.), containing hydrochloric acid (1 ml.), was added. The solution was treated dropwise with a solution of sodium nitrite (0·3 g.) in water (3 ml.) during 30 minutes. Dilution with water (10 ml.) and filtration gave *β-methyl-γ-nitrosotropolone* (0·268 g.), which crystallised from alcohol in plates, m. p. 178° (decomp.) (Found: C, 58·5; H, 4·5. $C_8H_7O_3N$ requires C, 58·2; H, 4·3%), giving a brown ferric test.

Reduction of β-methyl-γ-nitrosotropolone. The above nitroso-compound (0·11 g.) was reduced in alcohol (30 ml.) in the presence of 5% palladium—charcoal catalyst (0·05 g.). Hydrogen (30 ml., 2 mols.) was absorbed and, on concentration of the solution, yellow prisms were deposited (0·06 g.). Crystallisation from alcohol gave γ-amino-β-methyltropolone, m. p. 224° (decomp.), alone or mixed with an authentic sample. Preparation of the benzylidene derivative confirmed the identity.

α′-Amino-β-methyltropolone (I; R = H, R′ = NH_2).—β-Methyl-α′-nitrotropolone (0·22 g.) in dioxan–alcohol (30 ml.; 1 : 1) was shaken with 5% palladium—charcoal (0·1 g.) in an atmosphere of hydrogen under atmospheric conditions. Hydrogen (82 ml., 3 mols.) was absorbed during about an hour. Removal of the catalyst and evaporation of the solvent gave a crystalline residue which was sublimed at 120°/10 mm. Crystallisation from a little alcohol gave yellow prisms of *α′-amino-β-methyltropolone* (0·16 g.), m. p. 136—137° (Found: C, 63·1; H, 6·0; N, 9·5. $C_8H_9O_2N$ requires C, 63·5; H, 6·0; N, 9·3%), which gave a deep green ferric test and dissolved in dilute alkali or acid to give yellow solutions.

α-Amino-β-methyltropolone (IV; R = NH_2).—β-Methyl-α-nitrotropolone (0·18 g.) was reduced in the same manner as above. Sublimation of the residue at 130°/11 mm. gave *α-amino-β-methyltropolone* (0·12 g.), which crystallised from water as pale yellow prisms, m. p. 150—151° (Found: C, 63·1; H, 6·2; N, 9·2%), which gave a deep green ferric colour and dissolved readily in dilute acid and alkali.

Diazotisation and Rearrangement of α′-Amino-β-methyltropolone.—α′-Amino-β-methyltropolone (0·04 g.) in N-sulphuric acid (3 ml.) was treated dropwise with sodium nitrite (0·03 g.) in water (0·5 ml.) at 0°. An orange solution immediately formed and treatment of a small portion with alkaline β-naphthol gave an intense red precipitate. The diazonium solution was gently warmed, whereupon decomposition occurred and a colourless suspension was produced. The precipitate (0·033 g.) was sublimed at 130°/11 mm. and crystallised from water to give colourless flat needles, m. p. 177° (Found: C, 63·1; H, 5·5. Calc. for $C_8H_8O_3$: C, 63·2; H, 5·3%), unchanged by admixture with a sample of 4-methylsalicylic acid (V; R = Me, R′ = H) prepared by alkali fusion of 4-methylsalicylaldehyde (Tiemann and Schotten, *loc. cit.*).

Diazotisation and Rearrangement of α-Amino-β-methyltropolone.—The α-amino-tropolone (0·035 g.) was treated as above and reacted similarly. The precipitate (0·028 g.) was sublimed at 130°/11 mm., and the sublimate separated from water as needles, m. p. 170—171° (Found: C, 63·6; H, 5·7%. Calc.

for $C_8H_8O_3$: C, 63·2; H, 5·3%), found to be identical with 6-methylsalicylic acid (V; R = H, R′ = Me) a sample of which was prepared from 2-methyl-6-nitrobenzonitrile by hydrolysis (Gabriel and Thieme, *loc. cit.*), reduction to the amino-acid by the usual catalytic method, and replacement of the amino-group by hydroxyl through the diazonium sulphate (Mayer and Schulze, *loc. cit.*).

Ultra-violet Absorption Spectra.—Ultra-violet absorption spectra were determined in methanolic solution, a Beckman Quartz Spectrophotometer being used. Ionisation of the nitro-tropolones was suppressed by addition of 0·1% of acetic acid to the methanolic solution. A summary of the results is given below. The figures given in italics represent points of inflection.

Substituent in β-methyltropolone.	$\lambda_{max.}$	log $\varepsilon_{max.}$	$\lambda_{max.}$	log $\varepsilon_{max.}$	$\lambda_{max.}$	log $\varepsilon_{max.}$
γ-NH_2	2370	4·38	3600	4·12	3880	4·17
α-NH_2	2570	4·56	3350	4·02	3980	3·93
α′-NH_2	2560	4·51	3390	4·10	4060	3·90
γ-NO_2	2320	4·39	*2370*	*4·34*	3550	3·92
α-NO_2	2400	4·46	3200	3·83	3620	3·76
α′-NO_2	2450	4·42	3170	3·69	3750	3·78
γ-I	2370	4·37	3360	4·04	*3790*	*3·64*
γ-OH	2420	4·49	3350—3700	constant at 3·99		
Substituent in salicylic acid.						
6-Me	2400	3·75	3070	3·52		
4-Me	2380	3·90	2970	3·64		

Our thanks are due to the University of Western Australia for a Hackett Research Studentship (to P. R. J.), and to Imperial Chemical Industries Limited for a grant which defrayed some of the expenses of this investigation.

THE UNIVERSITY, SHEFFIELD, 10. [*Received, April 28th*, 1951.]

---

460. *New Syntheses of Cystine.*

By J. C. CRAWHALL and D. F. ELLIOTT.

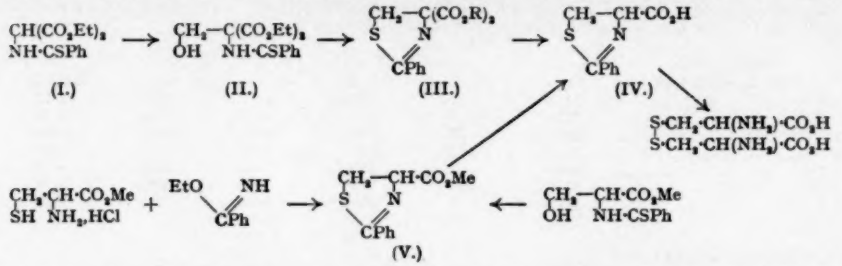
Serine * was converted into *N*-thiobenzoylserine methyl ester which gave methyl 2-phenyl-Δ^2-thiazoline-4-carboxylate on treatment with thionyl chloride. Hydrolysis of the thiazoline derivative yielded cystine. This method of replacing a hydroxyl group by a thiol group was utilised in the synthesis of cystine from aminomalonic ester. This ester was converted into thiobenzamidomalonic ester and into ethyl *N*-dithiocarbobenzyloxy-aminomalonate. These substances were condensed with formaldehyde, and the products converted by the action of thionyl chloride into thiazolines from which cystine was obtained.

IT was recently found that replacement of the β-hydroxyl group by a thiol group occurred when *N*-thiobenzoylserine methyl ester was treated with thionyl chloride (Elliott, *Nature*, 1948, **162**, 658). The good yield obtained and the simplicity of the procedure prompted a more detailed investigation of the reaction for synthetic purposes. Cystine has now been synthesised from aminomalonic ester by two related routes, this replacement reaction being used at an intermediate stage. The β-carbon atom of the cystine molecule was introduced by aldol condensation of formaldehyde with a thioacylaminomalonic ester, a reaction which gave excellent yields as in the case of the synthesis of serine from acetamidomalonic ester described by King (*J. Amer. Chem. Soc.*, 1947, **69**, 2738). This method of introducing a carbon atom is also valuable because it provides a convenient route to cystine containing a radioactive β-carbon atom.

Aminomalonic ester was conveniently purified and stored as its hydrochloride from which thiobenzamidomalonic ester (I) was prepared by reaction with (thiobenzoylthio)acetic acid and aqueous alkali according to Holmberg's method (Thé Svedberg Anniversary Volume, p. 299, Uppsala: Almquist and Wiksellis, 1944). It was later found more convenient to carry out this reaction in pyridine with use of triethylamine as a base. Addition of formaldehyde

* All substances containing asymmetric carbon atoms described in this paper were the DL-isomers.

to the thiobenzoyl compound (I) proceeded smoothly to give ethyl α-carbethoxy-β-hydroxy-α-thiobenzamidopropionate (II) in almost theoretical yield. In this condensation pyridine was used as a solvent and catalyst, a method due to Arnstein (*Nature*, 1949, **164**, 361) which is more convenient, when dealing with substances sparingly soluble in water, than the aqueous medium used by King (*loc. cit.*). When the thiobenzoyl compound (II) was added to ice-cold thionyl

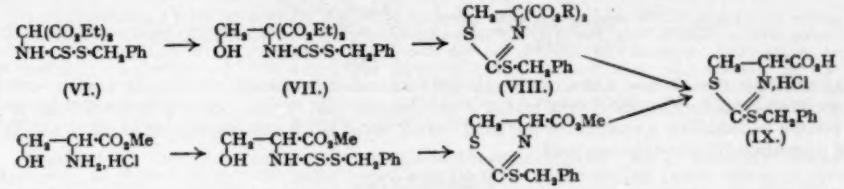


chloride an immediate liberation of gas took place, but it was found that the yield of 4 : 4-dicarbethoxy-2-phenyl-Δ^2-thiazoline (III) was greatly reduced if the reaction mixture was not kept for 30 minutes after the reaction had apparently ceased. It is possible that an intermediate chlorosulphinic ester was produced and cyclised relatively slowly to the thiazoline (III). Indirect evidence in favour of the formation of a compound of this type in related cyclisation reactions was obtained during some experiments on the synthesis of threonine (Elliott, *J.*, 1949, 589). The thiazoline ester (III) appeared to be very feebly basic, a fact which might be explained by the proximity of the carbethoxy-groups to the nitrogen atom, and no solid derivatives were obtained from it. Hydrolysis of the ester groups occurred very rapidly when alcoholic sodium hydroxide was added to the thiazoline ester, and produced a precipitate of the disodium salt (III; R = Na) of the corresponding dicarboxylic acid. The free acid was evidently very unstable because treatment of the disodium salt with dilute acid yielded 2-phenyl-Δ^2-thiazoline-4-carboxylic acid (IV) with spontaneous liberation of carbon dioxide. The structure assigned to the acid (IV) was confirmed by its synthesis, as indicated in the preceding scheme, by two independent routes: (1) from thiobenzoylserine methyl ester as already briefly described by Elliott (*loc. cit.*); (2) from cystine methyl ester hydrochloride by condensation with ethyl benzimidate (compare Jacobsen, *Compt. rend. Trav. Lab. Carlsberg, Sér. Chim.*, 1947, **26**, No. 1) followed by mild alkaline hydrolysis. Acid hydrolysis of the thiazoline ester (V) or the acid (IV) followed by oxidation gave inactive cystine in good yield.

The preparation of (thiobenzoylthio)acetic acid from benzotrichloride by Holmberg's method (*Arkiv Kemi, Min. Geol.*, 1944, **17**, *A*, No. 23) was inconvenient because of the long time required, and we were unable to achieve the yield claimed by Holmberg. By a modified procedure it was possible to prepare the substance in 40% yield in one day. As the starting materials used in the preparation are cheap and accessible, the low yield obtained is not a serious disadvantage; other methods of preparing thiobenzamidomalonic ester were, however, investigated. These included reaction of benzamidomalonic ester with phosphorus pentasulphide and potassium polysulphide (compare Kindler, *Annalen*, 1923, **431**, 187), which gave some of the desired substance though its isolation was difficult, reaction of thiobenzamide with aminomalonic ester, which failed, and reaction of benzaldehyde and sulphur with aminomalonic ester (Kindler, *loc. cit.*), which also failed. The reaction of sulphur with benzylideneaminomalonic ester by Kindler's method (*loc. cit.*) was not investigated because the latter substance was obtained in poor yield. When this work had been completed a publication by Kjaer (*Acta Chem. Scand.*, 1950, **4**, 1347) appeared describing the preparation of (thiobenzoylthio)-acetic acid in 51·5% yield from bromobenzene by a Grignard reaction followed by condensation of the dithiobenzoic acid with sodium chloroacetate.

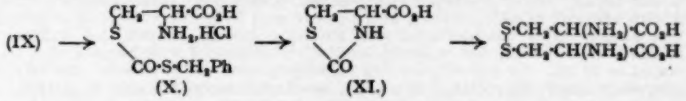
The initial difficulty experienced in the preparation of (thiobenzoylthio)acetic acid led to an investigation of another thioacyl derivative of aminomalonic ester. Cook, Harris, Heilbron, and Shaw (*J.*, 1948, 1056) prepared ethyl *N*-dithiocarbobenzyloxyaminomalonate (VI) by reaction of aminomalonic ester with carbon disulphide followed by alkylation with benzyl chloride in the presence of potassium hydroxide. This method did not give a good yield and it was found preferable to carry out both stages in pyridine solution in the presence of triethylamine. Condensation of the malonic ester derivative (VI) with formaldehyde gave an excellent

yield of ethyl α-dithiocarbobenzyloxyamino-α-hydroxymethylmalonate (VII), which was cyclised with thionyl chloride in the usual way. The product, 2-benzylthio-4 : 4-dicarbethoxy-Δ^2-thiazoline (VIII), like the related 2-phenyl-substituted thiazoline (III), did not form solid derivatives; it behaved similarly to (III) on alkaline hydrolysis also, giving the disodium salt (VIII; R = Na). Spontaneous decarboxylation occurred on acidification of the disodium



salt (VIII; R = Na), yielding an oily acid which formed a crystalline hydrochloride (IX). This substance was synthesised from serine methyl ester hydrochloride by a related series of reactions, as indicated in the scheme above, and its structure thereby confirmed.

The behaviour of the hydrochloride (IX) on acid hydrolysis was unexpected; no cystine was formed, the product being a crystalline substance which appeared to have resulted by addition of the elements of water to the starting material. This substance was assigned the structure (X) for three reasons: (1) it contained no free thiol groups; (2) it appeared to be the hydrochloride of a base, because it contained ionic chlorine, gave a ninhydrin reaction, and yielded a formyl derivative containing no chlorine; (3) above pH 7 it liberated toluene-ω-thiol and produced 2-ketothiazolidine-4-carboxylic acid (XI). *S*-Thiolcarbobenzyloxycysteine hydrochloride (X) was very resistant to acid hydrolysis, remaining largely unchanged after being heated for several hours with concentrated hydrochloric acid in a sealed tube at 160°. This resistance was later found to be attributable partly to the sparing solubility of the hydrochloride in concentrated hydrochloric acid; it was soluble in 6N-hydrochloric acid at the boiling point and slow hydrolysis occurred. The stability of compound (X) might result from the inhibition of the approach of hydrogen ions to the carbonyl group caused by the positively charged nitrogen atom in the vicinity (compare Neuberger and Moggridge, *J.*, 1938, 745;

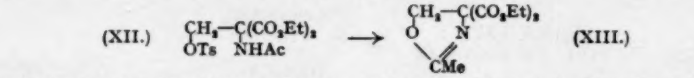


Synge, *Biochem. J.*, 1939, **33**, 1924). Attempts to bring about fission of the ester linkages by reaction of compound (X) with mercury salts under various conditions were not successful. An attempt to reduce the thiazoline (VIII; R = Et) with aluminium amalgam to a thiazolidine which would have been susceptible to mercuric chloride fission (Bentley, Catch, Cook, Heilbron, and Shaw, C.P.S. 267, September 15, 1944; "The Chemistry of Penicillin," p. 922, Princeton University Press, 1949) was also unsuccessful. The conversion of (X) into 2-ketothiazolidine-4-carboxylic acid (XI) under the influence of dilute alkali is probably analogous to the well-known rearrangement of *O*- to *N*-acylamino-alcohols under the same conditions. The reactions exemplified by the compounds (IX)—(XI) appear to be general for 2-alkylthiothiazolines and are being further studied.

In the synthesis of cystine by this method it was found preferable to proceed through compound (XI) rather than to carry out prolonged hydrolysis of the *s*-dithiocarbonic acid derivative (X). Acid hydrolysis of (XI), which was formed in quantitative yield from (X), occurred relatively rapidly. Although this route to cystine appears to be more involved than the synthesis from thiobenzamidomalonic ester, it is the more convenient method, it being possible to proceed from the disodium salt (VIII; R = Na) to cystine without isolation of any of the intermediates, whereas a very poor yield of cystine was obtained from the disodium salt (III) when intermediate isolation of the acid (IV) was omitted.

An unsuccessful attempt was made to synthesise cystine by Chapman and Owen's method (*J.*, 1950, 579) for preparing thiols from alcohols. Ethyl α-acetamido-α-carbethoxy-β-hydroxypropionate was converted into the corresponding toluene-*p*-sulphonic ester (XII), and when this reacted with potassium thiolacetate, formation of potassium toluene-*p*-sulphonate occurred,

but no substance containing a thiol group was detected after hydrolysis of the reaction product. It is possible that an oxazoline (XIII) was formed by the mechanism previously proposed for the cyclisation of *N*-benzoyl-*O*-toluene-*p*-sulphonyl*allo*threonine ethyl ester (Attenburrow, Elliott, and Penny, *J.*, 1948, 310) in the presence of potassium acetate, the only difference in the present example being the presence of thiolacetate ion instead of acetate ion. It is of



(XII.) (XIII.)

interest that Fry (*J. Org. Chem.*, 1950, **15**, 438) succeeded in opening the ring in 2-phenyl-Δ^2-oxazoline-4-carboxylic acid by the action of thiolbenzoic acid in pyridine to give *NS*-dibenzoylcysteine. Evidently a reaction of this kind did not occur in the present case although an excess of potassium thiolacetate was used.

Experimental.

(M. p.s are uncorrected.)

Aminomalonic Ester Hydrochloride.—The free base was prepared by Snyder and Smith's method (*J. Amer. Chem. Soc.*, 1944, **66**, 350) and the hydrochloride was formed by dissolution of the base in a large volume of dry ether and saturation with anhydrous hydrogen chloride (Levene and Schormüller, *J. Biol. Chem.*, 1934, **106**, 601); yield, 125 g. from 200 g. of malonic ester.

(Thiobenzoylthio)acetic Acid.—This compound has been prepared from benzotrichloride by Holmberg (*loc. cit.*). In our hands only a 40% yield could be obtained (cf. Kjaer, *loc. cit.*). Various attempts to improve this yield included the use of sodium sulphide instead of potassium sulphide in the reaction with benzotrichloride, the addition of alcoholic instead of aqueous sodium chloroacetate to the crude alkali salt of dithiobenzoic acid, and carrying out the reactions at the b. p.s of the solvents or under nitrogen. No improvement in yield could be effected, but the following method gave a 40% yield in 1 day instead of the 3 days necessary in Holmberg's method. A solution of potassium hydroxide pellets (7·5 g.) in ethanol (50 ml.) was divided into halves and one half was saturated with hydrogen sulphide which had been dried by passage through calcium chloride; the other half was then added to the first portion in a three-necked flask fitted with reflux condenser, nitrogen inlet, and dropping-funnel. A slow stream of nitrogen was passed through, the temperature was raised to 30°, and benzotrichloride (4·05 ml.; 5·6 g.) added dropwise at such a rate that the temperature did not rise above 60°. The mixture was then allowed to cool and remained for 2 hours at room temperature. Monochloroacetic acid (4 g.) was dissolved in water (25 ml.) and neutralised by addition of solid sodium carbonate, and the solution was added to the previous solution under nitrogen, and the mixture well shaken and then quickly raised to the b. p.; as soon as the colour change from brown to red had occurred (2—5 mins.) the solution was rapidly cooled (further heating caused considerable decomposition). The solution was diluted with water (100 ml.), acidified with concentrated hydrochloric acid, and extracted with benzene. The benzene layer was extracted with sodium carbonate solution, the sodium carbonate layer was acidified with concentrated hydrochloric acid and extracted with benzene, and the benzene layer evaporated to 10 ml. To this solution was added petroleum (b. p. 60—80°, 100 ml.), giving an instant precipitate of bright red plates (2·52 g., 41% based on benzotrichloride), m. p. 125°.

Thiobenzamidomalonic Ester.—(*a*) Aminomalonic ester hydrochloride (10 g.) was dissolved in pyridine (30 ml.), triethylamine (1 mol., 4·8 g.) and (thiobenzoylthio)acetic acid (11 g., 1·1 mol.) were then added, and the solution was shaken until the solid had dissolved. It was set aside overnight and then poured into excess of 2N-sulphuric acid containing some ice, and the mixture extracted with ether. The ethereal layer was extracted with dilute sodium hydrogen carbonate to remove excess of (thiobenzoylthio)acetic acid, leaving an olive-green ethereal solution which was dried (Na_2SO_4). Evaporation of the ether left an oil which solidified when scratched after addition of petroleum (b. p. 60—80°). The yield of *ethyl thiobenzamidomalonate*, m. p. 57°, was 11·6 g. (83%). Recrystallisation from ligroin raised the m. p. to 62° (Found: C, 56·8; H, 6·0; N, 5·0. $C_{14}H_{17}O_4NS$ requires C, 56·9; H, 5·8; N, 4·7%).

(*b*) Benzamidomalonic ester (4·0 g.) (Redemann and Dunn, *J. Biol. Chem.*, 1939, **130**, 341) was placed in a three-necked flask fitted with a stirrer and condenser closed by a calcium chloride tube. Dry xylene (30 ml.), phosphorus pentasulphide (0·96 g.), and liver of sulphur (1·52 g.) were added, and the temperature raised to 80—90° for 4 hours (cf. Kindler, *loc. cit.*). The red xylene solution was decanted from the undissolved material to which more dry xylene (20 ml.) was added, and heating and stirring at 90° were continued for 30 minutes. The xylene solution was again decanted and combined with the first extract, and the solution evaporated to dryness, leaving an oil which partly solidified. This was dissolved in aqueous alcohol, and after 4 days, well-defined needles (1·3 g.) of thiobenzamidomalonic ester had separated out; it had m. p. 61°, mixed m. p. with ester from (*a*) 61°.

Benzylideneaminomalonic Ester.—Benzaldehyde (3·2 g.) was added to aminomalonic ester (5 g.) in dry benzene (50 ml.), and the mixture refluxed for 4 hours, a Dean and Stark apparatus being used for the separation of the water formed. The solution, which smelt strongly of benzaldehyde, was extracted with concentrated aqueous sodium hydrogen sulphite. The benzene layer was evaporated to dryness, leaving the *diethyl* ester as an oil which had solidified after 3 days (4·2 g.), m. p. 96—101° (Found: N, 5·3. $C_{14}H_{17}O_4N$ requires N, 5·3%).

Ethyl α-Carbethoxy-β-hydroxy-α-thiobenzamidopropionate.—Thiobenzamidomalonic ester (4·42 g.) was dissolved in pyridine (4 ml.) and 39% aqueous formaldehyde (1·1 ml., 1 mol.) solution was delivered from a pipette under the surface of the solution, which was then left at 0° for 24 hours. The solution

was poured into a mixture of water and ether, and concentrated hydrochloric acid added until the aqueous layer was acid to Congo-red. The aqueous layer was thoroughly extracted with ether, and the ethereal layer washed with sodium hydrogen carbonate solution, dried (Na_2SO_4), and evaporated, leaving an oil which crystallised on cooling; the solid (4·53 g., 93%) had m. p. 106°. Recrystallisation from ligroin gave pure *ethyl α-carbethoxy-β-hydroxy-α-thiobenzamidopropionate* in the form of needles, m. p. 110° (Found: C, 55·4; H, 5·8; N, 4·1; S, 9·5. $C_{15}H_{19}O_3NS$ requires C, 55·4; H, 5·9; N, 4·3; S, 9·8%).

4 : 4-*Dicarbethoxy-2-phenyl-*Δ^2*-thiazoline.*—The foregoing ester (11·2 g.) was added in portions during 15 minutes to thionyl chloride (30 ml.; purified as described in *Org. Synth.*, Coll. Vol. II, p. 570) cooled in ice. After one hour at 0° the thionyl chloride was distilled off in a vacuum at 35°, the residual oil poured into a suspension of sodium hydrogen carbonate (50 g.) in water (100 ml.), and the mixture extracted with ether. The ethereal layer was dried and evaporated. The residual oil (10·15 g., 96%) was distilled and had b. p. 170°/0·05 mm. 4 : 4-*Dicarbethoxy-2-phenyl-*Δ^2*-thiazoline* was a very weak base, forming neither a picrate nor a chloroplatinate (Found: C, 58·8; H, 5·6; N, 4·6. $C_{15}H_{17}O_4NS$ requires C, 58·7; H, 5·5; N, 4·6%).

Disodium salt. This thiazoline (10·1 g.) was dissolved in ethanol (20 ml.), and a N-solution of sodium hydroxide in ethanol (31 ml., 2·2 mols.) added with shaking. The transient yellow colour at first produced was followed rapidly by a white precipitate. After 15 minutes, the microcrystalline *disodium* salt (7·35 g., 76%) was separated by centrifugation and dried in a vacuum desiccator (Found: N, 4·7; Na, 15·9. $C_{11}H_9O_4NSNa$ requires N, 4·7; Na, 15·7%).

2-*Phenyl-*Δ^2*-thiazoline-4-carboxylic Acid.*—(*a*) The foregoing disodium salt (2·4 g.) was covered with ethyl acetate, and N-hydrochloric acid (21 ml.) dropped into it with shaking until all the solid had dissolved. The ethyl acetate layer was washed three times with distilled water, dried, and evaporated. The residual oil (1 g., 60%) solidified, and was washed with ether and recrystallised from ethanol, giving 2-*phenyl-*Δ^2*-thiazoline-4-carboxylic acid*, m. p. 125—126°; mixed m. p., with a sample prepared as in (*b*), 123°.

(*b*) Methyl 2-phenyl-Δ^2-thiazoline-4-carboxylate (see below) (9 g.) was suspended in water (45 ml.) containing N-sodium hydroxide (45 ml., 1·1 mols.), and the mixture warmed to 50° until all the solid had dissolved. On cooling, the sodium salt of the corresponding acid crystallised and was dissolved by addition of water (20 ml.). N-Hydrochloric acid (45 ml.) was added, precipitating an oil which was extracted into ethyl acetate. The solvent was evaporated, and the crystalline acid (7 g.) purified from benzene–petroleum (b. p. 60—80°) (4 : 1). The acid (6 g.) had m. p. 122° (Found: C, 57·8; H, 4·6; N, 6·7; S, 15·7. $C_{10}H_9O_2NS$ requires C, 58·0; H, 4·4; N, 6·8; S, 15·5%).

Thiobenzoylserine Methyl Ester.—Serine methyl ester hydrochloride, prepared in the usual way from serine (0·5 g.), was dissolved in dry pyridine (3 ml.), and triethylamine (1·5 g., 3 mol.) added followed by (thiobenzoylthio)acetic acid (1·1 g.; 1·1 mols.) in pyridine (5 ml.). The mixture was left overnight and then poured into excess of 2N-sulphuric acid covered with a layer of ether. The ethereal layer was separated, the aqueous layer extracted again with ether, and the combined extracts were washed with sodium hydrogen carbonate, dried, and evaporated. The residue rapidly crystallised; the solid (0·86 g., 76% based on serine) had m. p. 84—85°. After recrystallisation from benzene the *thiobenzoylserine methyl ester* had m. p. 88° (Found: N, 5·8. $C_{12}H_{13}O_3NS$ requires N, 5·9%). This compound was also prepared in 63% yield from serine methyl ester hydrochloride by using aqueous sodium hydroxide as a base, according to Holmberg's method (*loc. cit.*).

Methyl 2-Phenyl-Δ^2*-thiazoline-4-carboxylate.*—(*a*) Thiobenzoylserine methyl ester (12·6 g.) was added in portions during 20 minutes to purified thionyl chloride (30 ml.) cooled in ice. After 30 minutes, the thionyl chloride was distilled off in a vacuum at 35°. The residue of *methyl 2-phenyl-*Δ^2*-thiazoline-4-carboxylate hydrochloride* (yield 93%) was crystallised from chloroform–ether and had m. p. 113—114° (Found: N, 5·55. $C_{11}H_{12}O_2NClS$ requires N, 5·4%). To prepare the free base, the same amount of crude hydrochloride was covered with a layer of ether and hydrated sodium acetate (5·94 g., 2 mols.) in water (20 ml.) was added, the mixture shaken, and the ethereal layer separated. After being washed with sodium hydrogen carbonate solution, the ethereal layer was dried and passed through a short column of alumina to remove impurities. The eluate was evaporated to dryness, leaving a crystalline solid, m. p. 67—68° (7·4 g., 64% based on thiobenzoylserine methyl ester). After recrystallisation from ligroin *methyl 2-phenyl-*Δ^2*-thiazoline-4-carboxylate* had m. p. 69° (Found: N, 6·0; S, 14·0. $C_{11}H_{11}O_2NS$ requires N, 6·3; S, 14·5%).

(*b*) Cysteine (20 g.) was suspended in dry methanol (150 ml.), and a stream of nitrogen passed through the solution. A rapid stream of dry hydrogen chloride was passed in until the solution boiled. It was then cooled, saturated with hydrogen chloride, and left overnight. The methanol was evaporated under reduced pressure in an atmosphere of nitrogen, the residue was dissolved in distilled water (40 ml.) with nitrogen passing through, and aqueous ammonia (*d* 0·88) added until the pH was raised to 3. Ethyl benzimidate (Elliott, *Biochem. J.*, 1949, **45**, 429) (30 g.) in ether (100 ml.) was then added, and the mixture shaken overnight. The two layers had emulsified next day, so more water was added and the layers were separated by centrifugation. The aqueous layer was extracted with ether, and the ethereal layers combined, dried, and evaporated. The residual oil was distilled under reduced pressure. The lower-boiling fraction was discarded and the fraction, b. p. 140°/0·05 mm., was collected. This solidified and was crystallised from ligroin; the solid (20 g.) had m. p. 68°. The mixed m. p. with the thiazoline methyl ester prepared as in (*a*) was 68°.

Cystine.—2-Phenyl-Δ^2-thiazoline-4-carboxylic acid or its methyl ester (1 g.) was refluxed with 3N-hydrochloric acid (25 ml.) for 4 hours, and the solution cooled and extracted twice with ether. The aqueous layer was evaporated to dryness, and the residual oil dissolved in N-hydrochloric acid (5 ml.) and titrated at 0° with 0·1N-iodine solution; 42·5 ml. were required (calc.: 48·5 ml.). The slight excess of iodine was removed with sodium thiosulphate solution, the pH was adjusted to 5 with sodium

hydroxide, and hydrated sodium acetate (0·2 g.) added. The solution then had pH 5·7. After two days at 0° the inactive cystine (0·32 g.) was filtered off. The aqueous filtrate was evaporated to dryness and after extraction with alcohol the residue was dissolved in hot water (15 ml.) which on cooling gave a further quantity of cystine (0·08 g.). Microbiological assay showed that this material had 50% of the growth-promoting activity of L-cystine for *Leuconostoc mesenteroides* P. 60.

Ethyl N-Dithiocarbobenzyloxyaminomalonate (cf. Cook *et al.*, *loc. cit.*).—Aminomalonic ester hydrochloride (3·7 g.) was dissolved in pyridine (12 ml.) which had been dried by distillation over sodium hydroxide, and triethylamine (3·46 g.) was added. Instantaneous precipitation of triethylamine hydrochloride occurred. Carbon disulphide (2 ml., 2 mols.) was added dropwise with shaking at 0°, and the solution kept at 0° for 2 hours. Benzyl chloride (2 ml., 1 mol.) was then added, and the solution kept at 0° overnight. The solution was poured into water and acidified with concentrated hydrochloric acid, and the oil extracted with ether. The ether layer was washed with sodium hydrogen carbonate solution, dried, and evaporated, leaving an oil which solidified when scratched; yield 5·2 g. (88%), m. p. 70°.

Isolation of the Intermediate Triethylamine Salt of N-Dicarbethoxymethyldithiocarbamic Acid.—Aminomalonic ester (3 g.) was mixed with triethylamine (1·73 g.) and cooled to −4° and carbon disulphide (1 ml.) was added dropwise with vigorous shaking. The resulting oil was cooled to −60° and scratched vigorously under anhydrous ether. The colourless needles, m. p. 50° (decomp.), of the *triethylamine* salt were rapidly filtered off and washed thoroughly with cold anhydrous ether to remove colouring matter (Found: C, 48·0; H, 8·0; S, 17·9; N, 7·9. $C_{16}H_{32}O_4N_2S_2$ requires C, 47·6; H, 7·9; S, 18·2; N, 7·9%).

Ethyl α-Dithiocarbobenzyloxyamino-α-hydroxymethylmalonate.—Ethyl *N*-dithiocarbobenzyloxyaminomalonate (7·3 g.) was dissolved in dry pyridine (7 ml.), aqueous formaldehyde solution (36·7%; 3·0 ml., 1·1 mols.) added, and the solution set aside overnight, then poured into water and acidified with concentrated hydrochloric acid, liberating an oil which was extracted into ether. The ethereal layer was washed with sodium hydrogen carbonate solution, dried, and evaporated. The residual oil crystallised when scratched after addition of petroleum. The solid (6·83 g., 86%) had m. p. 80°, raised by repeated recrystallisations from benzene–petroleum (b. p. 60—80°) (1 : 3) or from aqueous alcohol to 89° (Found: C, 50·7; H, 5·4; N, 3·7. $C_{14}H_{21}O_5NS_2$ requires C, 51·4; H, 5·6; N, 3·8%). The crude *ester* was suitable for the next stage.

2-Benzylthio-4 : 4-dicarbethoxy-Δ²-thiazoline and Disodium 2-Benzylthio-Δ²-thiazoline-4 : 4-dicarboxylate.—The preceding ester (15 g.) was added during 15 minutes to purified thionyl chloride (30 ml.), cooled in ice, and the reaction mixture kept at 0° for 1 hour. Excess of thionyl chloride was removed under reduced pressure at 35°, and the residual oil was poured into a suspension of sodium carbonate (70 g.) in water (150 ml.) covered with a layer of ether. The aqueous layer was thoroughly extracted with ether, and the combined extracts were dried and evaporated. The yield of 2-benzylthio-4 : 4-dicarbethoxy-Δ²-thiazoline was 13·45 g. (95%). Like the corresponding 2-phenyl derivative, this compound did not form a picrate and no attempt was made at distillation. It was used in the crude state for the next stage.

The crude diethyl ester (2·6 g.) was dissolved in alcohol (7 ml.), and N-alcoholic sodium hydroxide (9·4 ml., 2·1 mols.) added, producing a copious white precipitate within a few minutes. The solid was removed by centrifugation, washed with alcohol and ether by centrifugation, and dried in a vacuum desiccator (yield 1·7 g., 65%). *Disodium 2-benzylthio-Δ²-thiazoline-4 : 4-dicarboxylate* was purified by precipitation from an aqueous solution with ethanol (Found: N, 3·95; S, 17·4; Na, 14·8. $C_{12}H_9O_4NS_2Na_2$ requires N, 4·1; S, 18·8; Na, 13·5%).

S-Thiolcarbobenzyloxycysteine Hydrochloride (X).—The foregoing disodium salt (26 g.) was treated with 6N-hydrochloric acid (130 ml.). When effervescence had ceased the solution was heated under reflux for 30 minutes and cooled at 0° for 2 hours, and the coarse white precipitate (18 g., 77%), m. p. 173° (decomp.), filtered off. It was crystallised from 6N-hydrochloric acid, giving the pure *hydrochloride*, m. p. 183° (decomp.) (Found: C, 43·1; H, 4·7; N, 4·8. $C_{11}H_{14}O_3NClS$ requires C, 43·0; H, 4·6; N, 4·6%). The amino-acid when run on a paper chromatogram in phenol gave a weak spot, R_F 0·72. It was found that complete hydrolysis of this substance required at least 70 hours at the b. p. in the presence of 6N-hydrochloric acid.

N-Formyl-S-thiolcarbobenzyloxycysteine.—The above cysteine derivative (0·31 g.) was suspended in 90% formic acid (1·5 ml.) containing hydrated sodium acetate (0·2 g.), and the solution warmed to 40°. Acetic anhydride (0·5 ml.) was then added dropwise, and after the addition the solution was kept at 80° for 30 minutes. The solvent was then evaporated, and the residue leached with ether, giving the *N-formyl* compound in crystalline plates, m. p. 145—150°, raised by recrystallisation from glacial acetic acid to 152° (mixed m. p. with starting material, m. p. 174°, was 150°) (Found: C, 48·1; H, 4·4; N, 5·0. $C_{12}H_{13}O_4NS$ requires C, 48·6; H, 4·4; N, 4·7%).

2-Ketothiazolidine-4-carboxylic Acid.—The hydrochloride (X) (1 g.), suspended in alcohol (30 ml.), was treated with N-sodium hydroxide (9·8 ml., 3 mols.) and after 30 minutes the solution was acidified with N-hydrochloric acid (9·8 ml.) and evaporated to dryness. The last traces of toluene-ω-thiol were removed by a second evaporation after addition of a small quantity of water. The residue was extracted repeatedly with ether and the combined extracts were evaporated to dryness, leaving a crystalline solid (0·48 g., 100%), m. p. 146—148°. It was recrystallised from ethyl acetate, giving pure *2-ketothiazolidine-4-carboxylic acid*, m. p. 155° (Found: N, 9·5. $C_4H_5O_3NS$ requires N, 9·5%), which was sparingly soluble in ether and more soluble in acetone. Acetone extraction of the crude product described above did not give satisfactory results.

The thiazolidone derivative was soluble in water, giving a solution which reacted acid to Congo-red paper, effervesced on addition of sodium hydrogen carbonate, and did not give a blue colour with ninhydrin. Hydrolysis experiments showed that for complete hydrolysis to cysteine it was necessary

to heat the thiazolidone derivative with excess of 6N-hydrochloric acid for 20 hours under reflux. Carbon dioxide was liberated during hydrolysis in an amount equivalent to the sulph-hydryl content of the solution. For preparative purposes isolation of (IX), (X), and (XI) can be omitted as shown below.

Cystine.—Disodium 2-benzylthio-Δ^2-thiazoline-4 : 4-dicarboxylate (2 g.) was heated under reflux for 2 hours with N-hydrochloric acid (17·5 ml.), the solution was allowed to cool, and 3N-sodium hydroxide solution added until the solution was strongly alkaline. It was then set aside for 20 minutes, acidified with concentrated hydrochloric acid (50 ml.), and heated under reflux for 20 hours. This solution was evaporated to dryness to remove the toluene-α-thiol present. The residue was thoroughly extracted with alcohol, and the extract oxidised with N-iodine solution, neutralised with pyridine, and kept at 0° for 2 hours. The yield of inactive cystine was 0·30 g. (42·5%). This material was found to be pure inactive cystine by microbiological assay and by paper chromatography.

Methyl 2-benzylthio-Δ^2-thiazoline-4-carboxylate Hydrochloride.—Serine methyl ester hydrochloride (3·68 g.) was dissolved in pyridine (16 ml.), the solution cooled to 0° in ice, and triethylamine (4·74 ml., 2 mols.) added. This was followed by dropwise addition of carbon disulphide (2 ml.). The reaction mixture was left at 0° for 4 hours, then benzyl chloride (2 ml.) was added, and the solution kept at 0° overnight. The product was poured into a mixture of ether and water, and the aqueous layer was acidified with concentrated hydrochloric acid and extracted again with ether. The ethereal extract was washed with dilute hydrochloric acid followed by sodium hydrogen carbonate solution, dried, and evaporated. The residual oil, which could not be crystallised, was added dropwise to purified thionyl chloride (2 ml.) cooled in ice, and the mixture kept for 30 minutes at 0°. The thionyl chloride was distilled off under reduced pressure at 35° and dry ether was added to the residual oil, which solidified when scratched. *Methyl 2-benzylthio-Δ^2-thiazoline-4-carboxylate hydrochloride* had m. p. 113° (Found : N, 5·0. $C_{12}H_{14}O_2NClS_2$ requires N, 4·6%).

2-Benzylthio-Δ^2-thiazoline-4-carboxylic Acid Hydrochloride.—(*a*) The foregoing ester was suspended in water (this caused some dissociation of the hydrochloride), and the pH adjusted to 7 with N-sodium hydroxide. The oil was extracted with ether, the ethereal extract evaporated, the residual oil dissolved in alcohol, and N-alcoholic sodium hydroxide (6·2 ml.) added. The mixture was kept for 2 days. The solution was evaporated to dryness, N-hydrochloric acid (10 ml.) added, and the solution extracted thoroughly with benzene (this was possible because of the feebly basic properties of the thiazoline-carboxylic acid). The benzene was evaporated, and the residual oil triturated with 6N-hydrochloric acid (2 ml.). The oil rapidly crystallised and *2-benzylthio-Δ^2-thiazoline-4-carboxylic acid hydrochloride*, m. p. 163°, separated (Found : N, 4·9; S, 22·3. $C_{11}H_{12}O_2NClS_2$ requires N, 4·7; S, 22·2%).

(*b*) Disodium 2-benzylthio-Δ^2-thiazoline-4 : 4-dicarboxylate (1 g.) was treated with 6N-hydrochloric acid (5 ml.), liberating an oil with the evolution of carbon dioxide. The oil solidified when scratched. The yield was 0·51 g. of the hydrochloride, m. p. 157°, raised by crystallisation from glacial acetic acid to 165°.

Comparison of the two samples of the acid hydrochloride was best carried out by converting them both into the sparingly soluble *S*-thiolcarbobenzyloxycysteine hydrochloride by heating under reflux for 10 minutes with 6N-hydrochloric acid. The cysteine derivative prepared from the disodium salt had m. p. 183°, that derived from serine had m. p. 184°, and the mixed m. p. was 183° (all m. p.s with decomp.).

Ethyl α-Acetamido-α-carbethoxy-β-toluene-p-sulphonyloxypropionate.—A solution of ethyl α-acetamido-α-carbethoxy-β-hydroxypropionate (King, *loc. cit.*; 1 g.) in anhydrous pyridine (10 ml.) was cooled to −5°, toluene-*p*-sulphonyl chloride (0·85 g.; 10% excess) added, and the mixture shaken until the solid had dissolved and then set aside overnight at −2° (compare Tipson, *J. Org. Chem.*, 1944, **9**, 235). Water (1 ml.) was then added dropwise with cooling at 0°, followed by an additional 4 ml. in one portion. The mixture was then poured into 2N-sulphuric acid (100 ml.), and after thorough mixing the gum was allowed to settle, and the aqueous liquor decanted. The gum was dissolved in chloroform, and the solution shaken with 2N-sulphuric acid, then with sodium hydrogen carbonate solution, dried, and evaporated. The residual oil solidified on addition of petroleum (b. p. 40—60°). The yield of *ethyl α-acetamido-α-carbethoxy-β-toluene-p-sulphonyloxypropionate* (m. p. 78°) was 1·85 g. (57·5%); the m. p. was raised by recrystallisation from aqueous alcohol to 81° (Found : N, 3·5; S, 7·2. $C_{17}H_{23}O_8NS$ requires N, 3·5; S, 8·0%).

Reaction of Ethyl α-Acetamido-α-carbethoxy-β-toluene-p-sulphonyloxypropionate with Potassium Thiolacetate.—The toluene-*p*-sulphonyl derivative (1 g.) and potassium thiolacetate (1 g.) were dissolved in anhydrous ethanol (20 ml.), and the mixture refluxed for 40 minutes and then kept overnight. The potassium toluene-*p*-sulphonate (0·4 g.; 80%) was filtered off and washed with a little alcohol and then with ether. The filtrate was evaporated to dryness, the residue was extracted with anhydrous ether, and the extract evaporated to dryness, leaving an oil (0·66 g.) to which was added N-sodium hydroxide in ethanol (10·8 ml.), and the solution was set aside overnight. The precipitate was separated by centrifugation and washed with alcohol and ether. The dry solid was treated with excess of 3N-hydrochloric acid, which caused instantaneous liberation of carbon dioxide. Iodine titrations showed that neither this solution nor the solution obtained after prolonged boiling of the solid with dilute acid contained more than a trace of sulph-hydryl.

The authors acknowledge the collaboration of Dr. H. R. V. Arnstein in the early stages of this investigation, and thank Miss K. R. de Bouk for the microbiological assay of cystine and Mr. A. D. Brownstone for valuable experimental assistance.

NATIONAL INSTITUTE FOR MEDICAL RESEARCH,
MILL HILL, LONDON, N.W. 7.

[*Received, May 2nd,* 1951.]

461. *Alkenylation employing Lithium Alkenyls. Part V.* The Formation and Some Reactions of* cis*-Propenyl-lithium.*

By E. A. Braude and J. A. Coles.

cis-Propenyl bromide in ether reacts readily with lithium to give *cis*-propenyl- and propynyl-lithium in proportions of about 5 : 1. The composition of the mixture of lithium derivatives follows from that of their condensation products with carbonyl compounds and throws some light on the nature of the metalation reaction.

Treatment of the mixture of lithium derivatives with carbon dioxide yields mainly dipropenyl ketone and tetrolic acid, and reaction with benzaldehyde, acraldehyde, and crotonaldehyde affords 30—40% yields of the expected *cis*-propenylcarbinols, together with 5—10% yields of the corresponding propynylcarbinols. The structures of the *cis*-propenylcarbinols are established by catalytic hydrogenation, by their infra-red and ultra-violet light-absorption properties, and by synthesis by partial catalytic hydrogenation of the propynylcarbinols. The selective semi-hydrogenation of the propynyl group in propynylvinylcarbinol is, however, difficult to effect and the method of direct alkenylation is superior.

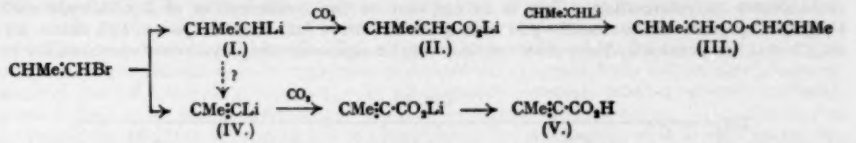
In previous papers (*J.*, 1950, 2000—2019; 1951, 1755) the preparation and some reactions of *iso*butenyl-, *cyclo*pentenyl-, and *cyclo*hexenyl-lithium have been described. The only other alkenyl-lithium at present known is styryl-lithium (Wright, *J. Org. Chem.*, 1936, **1**, 457). In order to establish the fact that formation of lithium derivatives is not limited to ββ-disubstituted and cyclic alkenyl halides which cannot easily undergo dehydrohalogenation, and to 2-arylvinyl halides which also yield Grignard derivatives, the preparation of propenyl-lithium, Me·CH:CHLi, was chosen as the next example for investigation.

Propenyl bromide can be prepared by the general method employed for *iso*butenyl bromide (Part III, *loc. cit.*), namely, simultaneous dehydrobromination and decarboxylation of the corresponding dibromocarboxylic acid, in this case 1 : 2-dibromobutyric acid, with sodium carbonate or pyridine. The propenyl bromide obtained by either procedure consists mainly of the isomer, b. p. 58—59°, together with a small proportion of the isomer, b. p. 63—64° (cf. Wislicenus and Langbein, *Annalen*, 1888, **248**, 325; Chavanne, *Compt. rend.*, 1914, **158**, 1698). Wislicenus and Langbein (*loc. cit.*) regarded the lower-boiling isomer as the *trans*-isomer, while Chavanne (*loc. cit.*) regarded it as the *cis*-isomer on the basis of its lower m. p. and b. p. and of its faster reaction with alcoholic potassium hydroxide. These assignments are clearly inconclusive, but the *cis*-configuration of the lower-boiling isomer can be inferred from dipole moment data. It has been shown by Hannay and Smyth (*J. Amer. Chem. Soc.*, 1946, **68**, 1005), from a consideration of contributing resonance structures, that the moment of a *cis*-propenyl halide would be expected to be similar to that of the *iso*propenyl halide, whereas the moment of the corresponding *trans*-propenyl halide should be higher, and that this expectation is fulfilled for the three propenyl chlorides. In the propenyl bromide series, only the moments of the propenyl bromide, b. p. 58°, and of *iso*propenyl bromide have been measured (Rogers, *J. Amer. Chem. Soc.*, 1947, **69**, 1243), but the closeness of the values (μ = 1·57 and 1·510 D., respectively) leaves no doubt that the lower-boiling propenyl bromide is the *cis*-isomer.

cis-Propenyl bromide, when carefully purified by fractionation, reacted rather more readily than *iso*butenyl bromide with lithium in ether, reaction being complete after 2—3 hours. Treatment of the resulting solution with excess of solid carbon dioxide yielded dipropenyl ketone (III) (20%) and tetrolic acid (V) (6%) as the main products. The ketone was characterised as the 2 : 4-dinitrophenylhydrazone and its skeletal structure was established by catalytic hydrogenation to di-*n*-propyl ketone and by its ultra-violet light absorption [maxima at 2450 (ε = 16,000) and 3360 A. (ε = 55)] which is typical of a dialkenyl ketone (cf. Part IV, *J.*, 1950, 2014). The predominant formation of ketones has previously been observed in the carboxylation of *iso*butenyl-, *cyclo*pentenyl-, and *cyclo*hexenyl-, but not of styryl-lithium, and must in this case proceed *via* the lithium salt (II) of *cis*-crotonic acid; the latter, though not isolated, was almost certainly present amongst the carboxylation products. The tetrolic acid must be derived from propynyl-lithium (IV); this may be formed either by the direct dehydro-

* Part IV, *J.*, 1950, 2014.

bromination of propenyl bromide or by the elimination of lithium hydride from propenyllithium (cf. Ziegler and Gellet, *Annalen*, 1950, **567**, 179), followed by further reaction of the resulting propyne with lithium.



In agreement with previous experience, the yields of carboxylation products are rather lower than those obtained in the reaction with other carbonyl compounds. The results obtained in the reaction with benzaldehyde (see below) indicate that, under optimum conditions, *cis*-propenyl bromide is converted into a mixture of propenyl- and propynyl-lithium in a proportion of 5 : 1 and in a total yield of not less than 50%. The proportion of ethylenic to acetylenic derivative is very similar to that observed by Wright (*loc. cit.*) for the corresponding reactions of β-bromostyrene but, in contrast to the behaviour of the latter bromide and of *iso*butenyl bromide (Part I, *loc. cit.*), direct metalation of propenyl bromide is not accompanied by the formation of the expected Wurtz reaction by-product, hexa-2 : 4-diene.

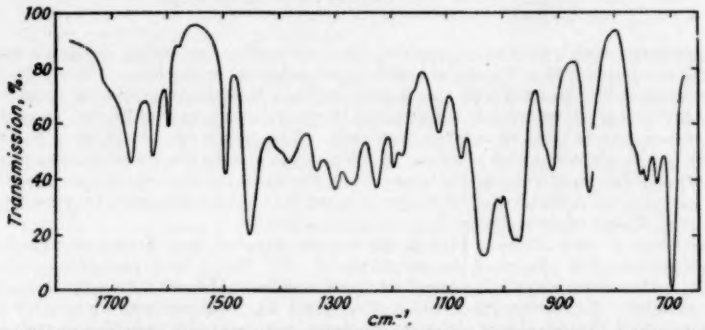
The reaction of the mixture of lithium derivatives obtained from *cis*-propenyl bromide with benzaldehyde afforded phenyl-*cis*-propenylcarbinol (VI) (35%) and phenylpropynylcarbinol (VII) (7%). The latter was also prepared by reaction of benzaldehyde with propynylmagnesium bromide (Iotsitch, *J. Russian Phys. Chem. Soc.*, 1909, **41**, 540) and was characterised by the *p*-nitrobenzoate. The structure of the ethylenic carbinol was established by catalytic hydrogenation (1 mol. of hydrogen) to 1-phenylbutanol and by the fact that it forms a nitrobenzoate (m. p. 57°) different from that (m. p. 99°) of the higher-boiling *trans*-isomer obtained by reaction of crotonaldehyde with phenylmagnesium bromide (Kenyon, Partridge, and Philipps, *J.*, 1937, 207; Braude, Jones, and Stern, *J.*, 1946, 396). The geometrical configuration of the higher-boiling isomer follows from the fact that the propenyl group in ordinary crotonaldehyde has a *trans*-configuration (Young, *J. Amer. Chem. Soc.*, 1932, **54**, 2498; Grédy and Piaux, *Compt. rend.*, 1934, **198**, 1235; Bentley, Everard, Marsden, and Sutton, *J.*, 1949, 2957). The configuration of the lower-boiling isomer was confirmed by its synthesis by partial hydrogenation of phenylpropynylcarbinol in the presence of platinum oxide. It is well known that catalytic hydrogenation results in the *cis*-addition of two hydrogen atoms and that the semihydrogenation of an acetylenic derivative produces only the *cis*-olefinic derivatives unless the latter is unstable (cf. Campbell and Campbell, *Chem. Reviews*, 1942, **31**, 148; Sondheimer, *J.*, 1950, 877; Raphael and Sondheimer, *J.*, 1950, 115). The catalyst usually preferred for semihydrogenation of an acetylenic linkage is palladium (cf. Heilbron, Jones, McCombie, and Weedon, *J.*, 1945, 84) and the use of platinum oxide in the present case was accidental; however, on interruption of the hydrogenation after 1 molecular equivalent had been absorbed, an excellent yield of the *cis*-propenylcarbinol was obtained and platinum oxide thus appears to display the same selectivity as other catalysts.

(VI.) Ph·CH(OH)·CH:CHMe Ph·CH(OH)·C:CMe (VII.)

The configuration of the propenyl group in the stereoisomeric phenylpropenylcarbinols was confirmed by infra-red light absorption date, kindly determined by Mr. A. R. Philpotts and Mr. W. Thain (cf. *Nature*, 1950, **166**, 1028) and partly reproduced in Figs. 1*a* and 1*b*. The absorption curves of the two isomers show characteristic differences in the 500—2000-cm.$^{-1}$ range and contain two bands near 970 and 760 cm.$^{-1}$ which are much more intense with the *trans*- than with the *cis*-isomer. The 970-cm.$^{-1}$ band is probably to be ascribed to a deformation frequency of the C–O–H group (cf. Barnard *et al.*, *J.*, 1950, 915) which, in the *trans*-carbinols, overlaps with a deformation frequency of the *trans*-H–C=C–H group; similar bands and intensity differences are shown by other pairs of stereoisomeric ethylenic carbinols (Crombie and Harper, *J.*, 1950, 873, 1707, 1714; Sondheimer, *loc. cit.*). The 760-cm.$^{-1}$ band has been assigned to an aromatic C–H deformation frequency (Philpotts and Thain, *loc. cit.*), but the difference between the intensity of this band in the phenyl-*cis*- and -*trans*-propenylcarbinols is rather unexpected on this basis. It can be estimated from the data that the samples of phenyl-*cis*-propenylcarbinol prepared by either of the two routes described above contained less than 3% of the *trans*-isomer.

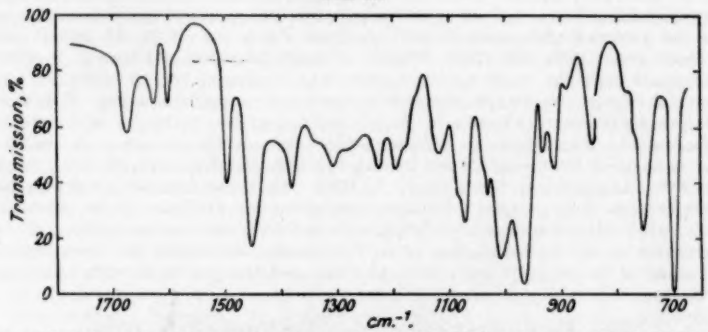
The reaction of the mixture of *cis*-propenyl- and propynyl-lithium obtained from *cis*-propenyl bromide with acraldehyde afforded *cis*-propenylvinylcarbinol (VIII) in 30% yield. None of the corresponding propynylcarbinol (IX) was isolated in this case and the reaction was attended by considerable polymerisation. This is in contrast to the condensation of acraldehyde with Grignard reagents which usually proceeds quite smoothly (cf. Braude, Jones, and Stern, *loc. cit.*), but it has previously been observed that vinyl compounds are polymerised more readily by

FIG. 1*a*.



Infra-red light absorption of phenyl-cis-propenylcarbinol in 20% *carbon tetrachloride* (1800—840 *cm.*$^{-1}$) *and* 10% cyclo*hexane* (840—600 *cm.*$^{-1}$) *solutions. Cell thickness* 0·013 *cm.*

FIG. 1*b*.



Infra-red light absorption of trans-*phenylpropenylcarbinol in* 20% *carbon tetrachloride* (1800—840 *cm.*$^{-1}$) *and* 10% cyclo*hexane* (840—600 *cm.*$^{-1}$) *solutions. Cell thickness* 0·013 *cm.*

lithium than by Grignard reagents (Ziegler *et al.*, *Annalen*, 1929, **473**, 57; 1934, **511**, 45). The structure of *cis*-propenylvinylcarbinol was proved by catalytic hydrogenation, which resulted

CHMe:CH·CH(OH)·CH:CH$_2$	CMe$\equiv$C·CH(OH)·CH:CH$_2$	CHMe:CH·CHEt·OH
(VIII.)	(IX.)	(X.)

in the uptake of 2 moles of hydrogen to give *n*-hexan-3-ol and by the formation of an α-naphthylurethane (m. p. 86—88°) different from that (m. p. 96—98°) of *trans*-propenylvinylcarbinol obtained by the condensation of (*trans*-)crotonaldehyde with sodium acetylide and subsequent partial hydrogenation (Heilbron, Jones, McCombie, and Weedon, *loc. cit.*).

In an attempt to synthesise *cis*-propenylvinylcarbinol by an alternative route, propynylmagnesium bromide was condensed with acraldehyde to give propynylvinylcarbinol and the latter was subjected to partial catalytic hydrogenation (one mole of hydrogen). When a 0·3% palladium–calcium carbonate catalyst was used, the product consisted of about equal

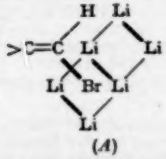
proportions of *cis*-propenylvinylcarbinol and ethyl-*cis*-propenylcarbinol (X) which are not readily separated by fractionation, while in the presence of 1·2% palladium-calcium carbonate or platinic oxide ethyl-*cis*-propenylcarbinol was the main product. The monoethylenic carbinol was characterised by an α-naphthylurethane, m. p. 75—76°, which is formed more readily than that of the diethylenic carbinol, and its structure was established by ozonisation, which afforded acetaldehyde but no formaldehyde. The structure was confirmed by an alternative synthesis in which propynylmagnesium bromide was condensed with propaldehyde to give ethylpropynylcarbinol, partial catalytic hydrogenation of which readily furnished ethyl-*cis*-propenylcarbinol, characterised by an α-naphthylurethane identical with that obtained before. The difficulty of achieving the selective hydrogenation of propynylvinylcarbinol shows that a vinyl group can effectively compete with a propynyl group under these conditions. No other examples of the semihydrogenation of a *di*-substituted acetylenic group in the presence of a vinyl group appear to have been described, but many cases of the selective semihydrogenation of a *mono*-substituted acetylenic (ethynyl) group in the presence of an alkenyl group are known. The ease of hydrogenation thus appears to decrease in the sequence R·C:CH > R·C:C·R > R·CH:CH$_2$ > R·CH:CH·R and it is possible to formulate the rule that in compounds containing two such groups selective hydrogenation can readily be effected only between non-adjacent members of the series. For this reason, as illustrated by the synthesis of *cis*-propenylvinylcarbinol, the method of direct alkenylation can offer considerable advantages even in the synthesis of ethylenic compounds which are structurally accessible through acetylenic intermediates.

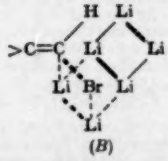
The reaction of the mixture of lithium derivatives from *cis*-propenyl bromide with crotonaldehyde afforded a somewhat better yield of products than that with acraldehyde and gave *cis-trans*-dipropenylcarbinol (XI) (40%) and *trans*-propenylpropynylcarbinol (XII) (7%), which

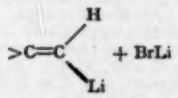
CHMe:CH·CH(OH)·CH:CHMe (XI.) CMe:C·CH(OH)·CH:CHMe (XII.)

were characterised by their α-naphthylurethanes. The skeletal structure of the dipropenylcarbinol was established by catalytic hydrogenation (two moles of hydrogen) to *n*-heptan-4-ol, which was oxidised to di-*n*-propyl ketone. The geometrical configuration of the ethylenic groups was not rigidly proved, but clearly follows from the work described above which shows that the propenyl group derived originally from *cis*-propenyl bromide will have the *cis*-configuration, whereas that derived from crotonaldehyde will have the *trans*-configuration.

The fact that the only ethylenic products obtained by reaction of the lithium derivatives of *cis*-propenyl bromide with aldehydes are the *cis*-propenylcarbinols is of considerable interest in relation to the mechanism of the metalation reaction. Clearly the metalation and condensation reactions may either be both accompanied by partial or complete *cis-trans*-isomerisation, in which case the formation of the *cis*-propenylcarbinols would have to be ascribed to their superior stability as compared with the *trans*-isomers, or else both steps must be accompanied by complete retention. The first possibility may be dismissed since the *trans*-isomers do not undergo *cis-trans*-isomerisation under conditions resembling those of the condensation reaction, as well as for various other reasons which need not be detailed. It must be concluded that both steps are accompanied by complete retention of geometrical configuration and that the direct metalation reaction gives rise exclusively to *cis*-propenyl-lithium.* It has sometimes been suggested that metalation processes are homolytic and involve "free"-radical intermediates (cf. Waters, "The Chemistry of Free Radicals," Oxford, 1946) but conventional mechanisms of this type are rendered unlikely by the present observation since they would be


(*A*)


(*B*)


(*C*)

expected to give rise to mixtures of geometrical isomers. In the absence of other decisive evidence, it is suggested that the entire reaction takes place on the surface of the metal as

* Wright (*loc. cit.*) states that carboxylation of the lithium derivative of *cis*-β-bromostyrene yields only *trans*-cinnamic acid and phenylpropiolic acid, but details of this experiment are not given and the stabilities of the bromide, and of *cis*-cinnamic acid, under the reaction conditions were not examined.

indicated on p. 2081 ($A \longrightarrow C$). The distance between neighbouring atoms in the lithium-metal crystal is considerably greater (*ca.* 3 A.) than the length of the carbon–bromine bond (*ca.* 1·5 A.), but in view of the large size and polarisability of the halogen atom, the proposed four-centre, planar transition state (*B*) is quite feasible and obviously accounts for the retention of geometrical configuration. The superior efficacy of lithium in this type of reaction may well be due to the fact that it has the smallest interatomic spacing amongst the alkali metals.

Experimental.

(M. p.s were determined on a Kofler block and are corrected.)

cis-*Propenyl Bromide.*—The literature concerning the preparation and properties of propenyl bromide are somewhat conflicting. In our hands, all the methods of preparation used give mainly *cis*-propenyl bromide, as described below.

(*a*) Bromine (1600 g.) was added dropwise to crotonic acid (820 g.) in carbon disulphide (1300 ml.) at 0°. Next morning, the solvent was distilled off and the crude dibromobutyric acid (m. p. 84°; 2200 g.) was carefully treated with excess of sodium carbonate (1500 g.) in water (5 l.). The resulting solution was steam-distilled and the product extracted with ether, dried ($CaCl_2$), and fractionated, giving mainly *cis*-propenyl bromide (180 g., 16%), b. p. 58°/760 mm., n_D^{24} 1·4542, in agreement with the results of Wislicenus and Langbein (*Annalen*, 1888, **248**, 325) and contrary to those of Farrell and Bachmann (*J. Amer. Chem. Soc.*, 1935, **57**, 1281) who state that no propenyl bromide is formed under these conditions. Only a small yield of propenyl bromide was obtained on heating dibromobutyric acid with excess of 2N-sodium hydroxide.

(*b*) A solution of dibromobutyric acid (500 g.) in dry pyridine (1 l.) was heated under reflux for 5 hours and then poured into excess of ice-cold hydrochloric acid. Isolation of the product as before and fractionation gave *cis*-propenyl bromide (43 g., 20%), b. p. 58°/760 mm., n_D^{22} 1·4533, in agreement with Farrell and Bachmann's results (*loc. cit.*).

An attempt to convert *cis*-propenyl bromide, b. p. 58°, into the *trans*-isomer, b. p. 63°, by the dehydrobromination of 1 : 1 : 2-tribromopropane with zinc in ethanol, as described by Wislicenus and Langbein (*loc. cit.*), failed, the *cis*-bromide again being obtained in agreement with Chavanne's results (*Compt. rend.*, 1914, **158**, 1698). Commercial samples of propenyl bromide also consisted almost entirely of *cis*-propenyl bromide, as judged by the b. p., but considerable variations were observed in n_D^{24} (1·4450—1·4550). Similar unexplained variations have been noted in the case of *iso*butenyl bromide (Part I, *J.*, 1950, 2000) where no stereoisomerism is possible. According to Chavanne (*loc. cit.*), pure *cis*-propenyl bromide has b. p. 58°, n_D 1·4564 (temperature not stated), whereas ordinary propenyl bromide is a 4 : 1 equilibrium *cis–trans*-mixture, which can be separated by prolonged fractionation in the presence of ethanol, but rapidly reverts to the equilibrium mixture on storage. The transformations described below, in which the bromide, b. p. 58°, is converted into *cis*-propenyl derivatives containing less than 2% of the *trans*-isomers, provide no evidence for the presence of the *trans*-bromide. However, the yields in these transformations are only of the order of 50% and it is possible that the *trans*-bromide, though present, is less readily metalated than the *cis*-bromide.

cis-*Propenyl-lithium.*—When freshly distilled from a trace of sodium, *cis*-propenyl bromide in dry ether solution reacts readily with lithium, under conditions previously described for *iso*butenyl bromide (Part I, *loc. cit.*). About one-tenth of the bromide is added initially and reaction sets in after 10—20 minutes. The remainder of the bromide is then added at a rate sufficient to maintain gentle refluxing of the ether and stirring is continued until all the metal has been consumed, usually 1—2 hours.

Dipropenyl Ketone and Tetrolic Acid.—Excess of solid carbon dioxide (300 g.) was added to the solution obtained by reaction of *cis*-propenyl bromide (65 g., 0·54 mol.) in ether (1 l.) with a stirred suspension of finely cut lithium metal (6·9 g., 1 mol.) in ether (1 l.). Stirring was continued for 3 hours. Saturated aqueous ammonium chloride (500 ml.) was then added, followed by 2N-hydrochloric acid (100 ml.). The ethereal layer was separated and extracted with saturated sodium hydrogen carbonate solution. The alkaline extract was acidified and the oily product crystallised from light petroleum (b. p. 60—80°) to give tetrolic acid (2·5 g., 6%), m. p. 76°, undepressed by an authentic specimen. The ethereal layer was dried (K_2CO_3) and fractionated to give *dipropenyl ketone* (*hepta-2 : 5-dien-4-one*) (4 g., 15%), a pale yellow liquid, b. p. 67—70°/20 mm., n_D^{21} 1·4837 (Found: C, 76·5; H, 9·5. $C_7H_{10}O$ requires C, 76·3; H, 9·1%). Light absorption in ethanol: $\lambda_{max.}$ 2450, 2510, and 3360 A.; ε = 15,900, 15,500, and 55, respectively. The ketone gave a 2 : 4-*dinitrophenylhydrazone*, which was chromatographed on alumina from benzene solution and crystallised from aqueous methanol in red prisms, m. p. 152° (Found: C, 53·6; H, 4·8; N, 18·6. $C_{13}H_{14}O_4N_4$ requires C, 53·8; H, 4·8; N, 19·3%). Light absorption in chloroform: $\lambda_{max.}$ 2580 and 3870 A., ε = 17,000 and 31,000 respectively.

Hydrogenation of dipropenyl ketone (1·7 g.) in methanol (25 ml.) in the presence of platinic oxide resulted in the uptake of 760 ml. of hydrogen at 18°/768 mm. (Calc., 800 ml.) to give heptan-4-one, identified as the 2 : 4-dinitrophenylhydrazone, which after chromatography on alumina from benzene solution and crystallisation from methanol had m. p. 74—75°, undepressed on admixture with an authentic specimen.

Phenyl-cis-*propenylcarbinol* (1-*Phenylbut-2-en-1-ol*) (VI) *and Phenylpropynylcarbinol* (1-*Phenylbut-2-yn-1-ol*) (VII).—(*a*) Benzaldehyde (53 g.) in ether (50 ml.) was gradually added at 0° to the solution obtained by treating *cis*-propenyl bromide (65 g.) with lithium (6·9 g.) in ether (1 l.). Stirring was continued for 2 hours and ice-cold saturated aqueous ammonium chloride (500 ml.) was then added.

The ethereal layer was separated, dried (Na_2SO_4–K_2CO_3) and fractionated through an 8-inch Fenske column to give cis-1-*phenylbut*-2-*en*-1-*ol* (24 g., 35%), b. p. 81°/0·2 mm., n_D^{21} 1·5412 (Found: C, 80·8; H, 8·1. $C_{10}H_{12}O$ requires C, 80·9; H, 8·2%) and 1-phenylbut-2-yn-1-ol (5 g., 7%), b. p. 88°/0·2 mm., n_D^{20} 1·5496. The two carbinols exhibited light absorption properties identical with those of the samples obtained under (*b*) and formed *p*-nitrobenzoates in good yields, m. p.s 56—57° and 104—105°, respectively, undepressed on admixture with the authentic specimens described below.

Hydrogenation of *cis*-1-phenylbut-2-en-1-ol (1·6 g.) in methanol (30 ml.) in the presence of platinic oxide resulted in the uptake of 250 ml. of hydrogen at 27°/768 mm. (Calc., 250 ml.). After removal of the catalyst and solvent, the product was dissolved in ether (10 ml.) and oxidised to *n*-butyrophenone by shaking it with potassium dichromate (1·6 g.) in 2N-sulphuric acid. The ketone was identified as the semicarbazone, which was crystallised from aqueous ethanol and had m. p. 189·5—190·5° (Tiffeneau and Levy, *Compt. rend.*, 1926, **183**, 920, give m. p. 188—189°), and the 2 : 4-dinitrophenylhydrazone, which was chromatographed on alumina from benzene solution and crystallised from ethyl acetate in red plates, m. p. 192—193° (Evans, *J.*, 1936, 785, gives 190°) undepressed on admixture with an authentic specimen.

(*b*) Benzaldehyde (53 g.) in ether (50 ml.) was gradually added to a solution of propynylmagnesium bromide, obtained by passing propyne (Hurd, Meinert, and Spence, *J. Amer. Chem. Soc.*, 1930, **52**, 1138) into a solution of ethylmagnesium bromide (from Mg, 12·2 g.) in ether (500 ml.) at 0°. After overnight stirring, ice-cold saturated aqueous ammonium chloride (600 ml.) was added. The ethereal layer was separated, dried (Na_2SO_4–K_2CO_3) and fractionated, giving 1-phenylbut-2-yn-1-ol (20 g., 30%), b. p. 110°/0·8 mm., n_D^{20} 1·5519, which solidified on cooling in plates, m. p. 37° (Iotsitch, *J. Russ. Phys. Chem. Soc.*, 1909, **41**, 540, gives b. p. 128°/9 mm., m. p. 30°). Light absorption in ethanol: $\lambda_{max.}$ 2510, 2570, and 2640 A.; ε = 370, 440, and 390, respectively. The carbinol formed a p-*nitrobenzoate* which crystallised from aqueous methanol in long prisms, m. p. 107° (Found: C, 69·5; H, 4·5; N, 4·7. $C_{12}H_{13}O_4N$ requires C, 69·2; H, 4·4; N, 4·75%).

1-Phenylbut-2-yn-1-ol (5·5 g., 0·038 mol.) in methanol (100 ml.) was hydrogenated in the presence of platinic oxide (10 mg.) until 900 ml. of hydrogen at 21°/768 mm. (corresponding to one mol.) had been absorbed. Removal of the catalyst and fractionation afforded *cis*-1-phenylbut-2-en-1-ol (4·8 g.), b. p. 81°/0·2 mm., n_D^{20} 1·5350. Ultra-violet light absorption in ethanol: $\lambda_{max.}$ 2550 A.; ε = 2000. Infra-red light absorption: see Fig. 1*b*. Treatment of a solution of the carbinol in dry pyridine with the calculated amount of *p*-nitrobenzoyl chloride at 0° gave the *p*-nitrobenzoate which crystallised from aqueous methanol in microcrystalline plates, m. p. 57—58° (Found: C, 69·0; H, 5·2; N, 4·9. $C_{17}H_{15}O_4N$ requires C, 68·7; H, 5·05; N, 4·7%). Light absorption of the *p*-nitrobenzoate in ethanol: $\lambda_{max.}$ 2650 A.; ε = 16,500.

cis-*Propenylvinylcarbinol* (*Hexa*-1 : 4-*dien*-3-*ol*) (VIII).—Acraldehyde (35 g.) in ether (50 ml.) was gradually added at 0° to the solution obtained by treating *cis*-propenyl bromide (65 g.) with lithium (6·9 g.) in ether (1 l.). After the mixture had been stirred overnight, saturated aqueous ammonium chloride (500 ml.) was added. Solid polymeric products (10 g.) were filtered off and the ethereal layer was separated, dried (Na_2SO_4–K_2CO_3), and fractionated, to give cis-*hexa*-1 : 4-*dien*-3-*ol* (15 g., 30%), b. p. 86—87°/87 mm., n_D^{27} 1·4559 (Found: C, 73·6; H, 10·1. $C_6H_{10}O$ requires C, 73·4; H, 10·25%). Light absorption in ethanol: ε = <200 between 2200 and 3000 A. The carbinol formed an *α-naphthylurethane* which crystallised from light petroleum (b. p. 80—100°) in needles, m. p. 86—88° (Found: N, 5·5. $C_{17}H_{17}O_2N$ requires N, 5·25%). A mixture of this derivative with *trans*-hexa-1 : 4-dien-3-ol α-naphthylurethane (m. p. 93·5—94·5; Heilbron, Jones, McCombie, and Weedon, *J.*, 1945, 84) melted at 89—91·5°.

Hydrogenation of the *cis*-dienol (1·3 g.) in methanol (30 ml.) in the presence of platinic oxide resulted in the uptake of 650 ml. of hydrogen at 23°/761 mm. (Calc., 645 ml.). After removal of the catalyst and solvent, the residue was taken up in ether (10 ml.) and shaken with potassium dichromate (1·3 g.) in 2N-sulphuric acid (30 ml.), and the product converted into ethyl *n*-propyl ketone 2 : 4-dinitrophenylhydrazone, which after chromatography on alumina from benzene solution and crystallisation from ethyl acetate had m. p. 128—130°, undepressed on admixture with an authentic specimen.

Propynylvinylcarbinol (*Hexa*-1-*en*-4-*yn*-3-*ol*) (IX).—Acraldehyde (28 g.) in ether (35 ml.) was added dropwise to a solution prepared as above, of propynylmagnesium bromide (from Mg, 12·2 g.) in ether (500 ml.) at 0° and the whole stirred overnight. Ice-cold saturated aqueous ammonium chloride (600 ml.) was then added. The ethereal layer was separated, dried (Na_2SO_4–K_2CO_3), and fractionated, giving *hexa*-1-*en*-4-*yn*-3-*ol* (18 g., 37%), b. p. 73°/26 mm., n_D^{21} 1·4712 (Found: C, 75·1; H, 8·5. C_6H_8O requires C, 74·9; H, 8·4%). Light absorption in ethanol: ε = <100 in the region 2200—4000 A. The *α-naphthylurethane* crystallised from light petroleum (b. p. 80—100°) in white clusters, m. p. 97—99° (Found: N, 5·6. $C_{17}H_{15}O_2N$ requires N, 5·3%).

Ethylpropynylcarbinol (*Hex*-4-*yn*-3-*ol*) *and Ethyl*-cis-*propenylcarbinol* (cis-*Hex*-4-*en*-3-*ol*) (X).—Freshly distilled propaldehyde (29 g.) in ether (50 ml.) was added dropwise to a solution, prepared as above, of propynylmagnesium bromide (from Mg, 12·2 g.) in ether (500 ml.) at 0°. After being stirred overnight, the reaction mixture was added slowly, with stirring, to ice-cold, saturated aqueous ammonium chloride (400 ml.). The ethereal layer was separated, dried (Na_2SO_4), and fractionated, giving *hex*-4-*yn*-3-*ol* (20 g., 40%), b. p. 51—52°/13 mm., n_D^{21} 1·4490 (Found: C, 73·2; H, 10·5. $C_6H_{10}O$ requires C, 73·4; H, 10·25%). Light absorption in ethanol: ε = <200 in the region 2200—4000 A. The *α-naphthylurethane* crystallised from light petroleum (b. p. 80—100°) in white clusters, m. p. 82—83° (Found: C, 75·9; H, 6·2; N, 5·6. $C_{17}H_{17}O_2N$ requires C, 76·3; H, 6·4; N, 5·6%).

The hexynol (2·5 g.) in methanol (20 ml.) was hydrogenated in the presence of a 1·2% palladium–calcium carbonate catalyst until 600 ml. (one mol.) of hydrogen at 16°/759 mm. had been absorbed.

Distillation of the product gave cis-*hex*-4-*en*-3-*ol* (2·2 g.), b. p. 44—46°/14 mm., n_D^{21} 1·4342 (Found: C, 72·0; H, 12·0. $C_6H_{12}O$ requires C, 72·0; H, 11·1%) (Airs, Balfe, and Kenyon, *J.*, 1942, 18, give b. p. 135°/760 mm., n_D^{15} 1·4325, for the *trans*-isomer). The carbinol formed an *α-naphthylurethane*, which crystallised from light petroleum (b. p. 80—100°) in clusters, m. p. 74—75° (Found: C, 76·2; H, 7·6; N, 5·5. $C_{17}H_{19}O_2N$ requires C, 75·8; H, 7·1; N, 5·3%).

Partial Hydrogenation of Propynylvinylcarbinol (*Hex*-1-*en*-4-*yn*-3-*ol*).—Hex-1-en-4-yn-3-ol (3·4 g.) in methanol (20 ml.) was hydrogenated in the presence of a 0·3% palladium–calcium carbonate catalyst until 820 ml. of hydrogen at 17°/765 mm. (corresponding to one mol.) had been absorbed (about 8 hours). The product was fractionated through a 3″ Fenske column and yielded a continuous range of fractions (total, 2·6 g.), b. p. 44—47°/12 mm., n_D^{24} 1·4420—1·4530, containing varying proportions of *cis*-hexa-1 : 4-dien-3-ol and *cis*-hex-4-en-3-ol, which were not effectively separated under these conditions. On treatment with α-naphthyl *iso*cyanate and a trace of triethylamine, both the lowest and highest fractions yielded only the α-naphthylurethane of *cis*-hex-4-en-3-ol, which was crystallised from light petroleum (b. p. 80—100°) and had m. p. 75—76°, undepressed on admixture with the authentic sample described above. The presence of the other carbinol in about equal proportion was proved by acid treatment of the carbinol mixture, which results in the isomerisation of hexa-1 : 4-dien-3-ol into hexa-3 : 5-dien-2-ol which can be separated more easily from the unchanged hex-4-en-3-ol (Braude and Coles, *J.*, 1951, 2085).

When the partial hydrogenation (one mol. of hydrogen) was carried out in the presence of a 1·3% palladium–calcium carbonate catalyst or platinic oxide, the uptake of hydrogen was much more rapid and the main product was hex-4-en-3-ol, identified by the α-naphthylurethane, m. p. 76—77°, undepressed on admixture with the sample described above, and very little *cis*-hexa-1 : 4-dien-3-ol was obtained. Ozonisation of hex-4-en-3-ol (0·5 g.) in carbon tetrachloride (20 ml.) for 4 hours and decomposition of the ozonide by the method of Church *et al.* (*J. Amer. Chem. Soc.*, 1934, **56**, 176) afforded acetaldehyde, isolated as the 2 : 4-dinitrophenylhydrazone (0·4 g., 45%), m. p. 164°, undepressed on admixture with an authentic specimen.

cis-trans-*Dipropenylcarbinol* (*Hepta*-2 : 5-*dien*-4-*ol*) (XI) *and* trans-*Propenylpropynylcarbinol* (*Hept*-2-*en*-5-*yn*-4-*ol*) (XII).—Crotonaldehyde (35 g.) in ether (50 ml.) was added dropwise at 0° to the solution obtained by treating *cis*-propenyl bromide (65 g.) with lithium (6·9 g.) in ether (1 l.). Stirring was continued for 2 hours and the solution was then treated with saturated aqueous ammonium chloride (600 ml.). The ethereal layer was separated, dried (Na_2SO_4–K_2CO_3), and fractionated through a 12″ Fenske column, to give (i) cis-trans-*hepta*-2 : 5-*dien*-4-*ol* (21 g., 38%), b. p. 72°/16 mm., n_D^{24} 1·4617 (Found: C, 75·4; H, 11·0. $C_7H_{12}O$ requires C, 75·0; H, 10·8%), and (ii) cis-*hepta*-2-*en*-5-*yn*-4-*ol* (4 g., 7%), b. p. 78°/16 mm., n_D^{22} 1·4690. Neither carbinol showed any light absorption with $\varepsilon = >500$ in the 2200—3000-A. region. The dienol formed an *α-naphthylurethane* which crystallised from light petroleum (b. p. 80—100°) in plates, m. p. 108° (Found: C, 76·7; H, 6·7; N, 5·2. $C_{18}H_{19}O_2N$ requires C, 76·9; H, 6·8; N, 5·0%). The heptenynol formed an *α-naphthylurethane* which crystallised from light petroleum (b. p. 100—120°) in plates, m. p. 132—133° (Found: C, 77·1; H, 6·2; N, 5·1. $C_{18}H_{17}O_2N$ requires C, 77·4; H, 6·1; N, 5·0%).

Hydrogenation of *cis-trans*-hepta-2 : 5-dien-4-ol (1·5 g.) in methanol (50 ml.) in the presence of platinic oxide resulted in the uptake of 700 ml. of hydrogen at 27°/688 mm. (Calc., 650 ml.). After removal of the catalyst and solvent, the residue was taken up in ether and oxidised with potassium dichromate (1·4 g.) in 2N-sulphuric acid, giving di-*n*-propyl ketone, b. p. 145°, identified by the 2 : 4-dinitrophenylhydrazone which after chromatography on alumina from benzene solution and crystallisation from aqueous methanol had m. p. 74°, undepressed on admixture with an authentic specimen.

We thank Professor R. P. Linstead, C.B.E., F.R.S., for his interest in the work described in this and the following paper, and the Department of Scientific and Industrial Research for a grant (to J. A. C.).

Imperial College of Science and Technology,
South Kensington, London, S.W.7.

[*Received, February 9th*, 1951.]

462. *Studies in Molecular Rearrangement. Part VII.* The Oxotropic Rearrangement of* cis-*Propenylcarbinols. The Stereochemical Course of Anionotropy.*

By E. A. Braude and J. A. Coles.

Three-carbon anionotropy in *cis*-ethylenic systems has been investigated for the first time, with particular reference to the stereochemical course of the reaction.

Phenyl-*cis*-propenylcarbinol (I*a*), like its *trans*-isomer (I*b*), rearranges under acidic conditions to give mainly, or exclusively, methyl-*trans*-styrylcarbinol (II*b*). *cis*-Methylstyrylcarbinol (II*a*) has been synthesized for comparison by partial hydrogenation of 4-phenylbut-3-yn-2-ol (III). Its infra-red and ultra-violet light absorption differ significantly from those of the *trans*-isomer and provide evidence for steric inhibition of hyperconjugation.

cis-Propenylvinylcarbinol (IV*a*), unlike its *trans*-isomer (IV*b*), rearranges to give mainly or exclusively *cis*-butadienylmethylcarbinol (V*a*), which is unreactive towards maleic anhydride. *cis-trans*-Dipropenylcarbinol (X*a*) rearranges to give a mixture of stereoisomeric hepta-3 : 5-dien-2-ols (XI). A possible explanation for the unexpected formation of the *cis*-rearranged isomers from (IV*a*) and (X*a*) is suggested, which involves a novel type of intramolecular interaction, termed "π-hydrogen bonding," between the *cis*-methyl and the vinyl group.

The results lend further support to the mechanism of anionotropy involving bimolecular γ-attack by a neutral molecule, and provide compelling evidence against the intervention of free carbonium ions.

Three-carbon anionotropy has been extensively investigated in recent years in this and other laboratories, but relatively little attention has hitherto been paid to the stereochemical aspects of such reactions. The systems most extensively studied involve migration of a hydroxyl group (three-carbon oxotropy) and for these the available stereochemical information may be summarised as follows : (*a*) rearrangement of optically active allyl alcohols in aqueous media is accompanied by extensive or complete racemisation (Kenyon, Partridge, and Phillips, *J.*, 1937, 207; Airs, Balfe, and Kenyon, *J.*, 1942, 18), the rate of which is equal to that of rearrangement (Braude and Jones, *J.*, 1944, 436; Kenyon and Poplett, *J.*, 1945, 273); (*b*) in the rearrangement of *trans*-propenylcarbinols, the new double bond formed is also mainly, or exclusively, *trans*. The evidence concerning (*b*) is circumstantial rather than conclusive and is mainly based on the following observations : (i) the phenylpropenylcarbinol (I*b*) obtained from crotonaldehyde and phenylmagnesium bromide has a *trans*-configuration (Braude and Coles, *J.*, 1951, 2078) and rearranges to a methylstyrylcarbinol (II*b*) which is identical with that obtained from cinnamaldehyde and methylmagnesium bromide (Braude, Jones, and Stern, *J.*, 1946, 396) and is now shown to have a *trans*-configuration; (ii) the propenylvinylcarbinol (IV*b*) obtained from crotonaldehyde (Heilbron, Jones, McCombie, and Weedon, *J.*, 1945, 88) has been shown to have the *trans*-configuration (Braude and Coles, *loc. cit.*) and rearranges to a butadienylmethylcarbinol (V*b*) which readily forms a maleic anhydride adduct in good yield (Heilbron *et al.*, *loc. cit.*) and may therefore be assumed to have a *trans*-configuration (D. Craig, *J. Amer. Chem. Soc.*, 1943, **65**, 1006; 1950, **72**, 1678; Petrov, *J. Gen. Chem. U.S.S.R.*, 1948, **18**, 1125; L. E. Craig and Larrabee, *J. Amer. Chem. Soc.*, 1951, **73**, 1192). Clearly, however, these results do not prove that only the rearranged *trans*-isomers are initially formed unless the corresponding rearranged *cis*-isomers are stable under the reaction conditions. It is relevant also that the formation of mixtures of rearranged *cis*- and *trans*-isomers has been considered (Braude and Jones, 1946, 122; Braude, Jones, and Stern, *loc. cit.*; Braude and Stern, *J.*, 1947, 1096) as one possible explanation of certain discrepancies in the ultra-violet light absorption of the products of some oxotropic rearrangements before and after their isolation from the reaction medium.

The present paper is concerned with a closer study of the stereochemical course of three-carbon oxotropy and of the influence of geometrical configuration in the starting compounds. The rearrangements of a number of 1 : 3-substituted allyl alcohols probably having the *cis*-configuration, since they were prepared by partial catalytic hydrogenation of the corresponding 1 : 3-substituted propargyl alcohols, have been described (cf. Nazarov and Fisher, *Bull Acad. Sci.*

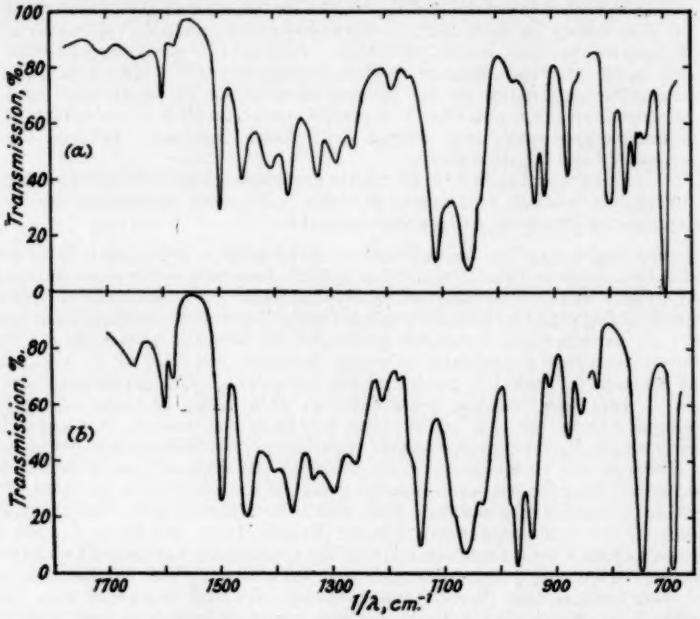
* Part VI, *J.*, 1951, 1755.

U.R.S.S., Cl. Sci. Chim., 1945, 631; 1948, 311, 427; 1949, 386; *J. Gen. Chem. U.S.S.R.*, 1950, **20**, 1107, 1114), but neither the stereochemical homogeneity of the starting materials, nor the stereochemical configuration of the products, was established. The synthesis of three stereochemically pure *cis*-propenylcarbinols described in the preceding paper provided us with an opportunity to compare, for the first time, the rearrangement of authentic geometrical isomers of known configuration.

Oxotropic Rearrangement of Phenyl-cis- *and* -trans-*propenylcarbinols.*—Phenyl-*cis*-propenylcarbinol (*cis*-1-phenylbut-2-enol) (I*a*), like its *trans*-isomer (I*b*), undergoes rearrangement in the presence of dilute acids in aqueous dioxan and is converted into methyl-*trans*-styrylcarbinol (*trans*-4-phenylbut-3-en-2-ol) (II*b*). The identity of the rearrangement products of (I*a* and *b*) was established by their ultra-violet and infra-red light absorption and by the formation of the same *p*-nitrobenzoate. The structure and configuration of methyl-*trans*-styrylcarbinol follows

FIG. 1.

Infra-red light absorption in 20% *carbon tetrachloride* (1800—840 *cm.*$^{-1}$) *and* 10% cyclo*hexane* (840—670 *cm.*$^{-1}$). *Cell thickness*, 0·013 *cm.* (*a*) *Methyl*-cis- *and* (b) -trans-*styrylcarbinol.*



from its alternative syntheses (Klages, *Ber.*, 1902, **35**, 2650; Wright, *J. Org. Chem.*, 1936, **1**, 457; Kenyon, Partridge, and Phillips, *loc. cit.*; Braude, Jones, and Stern, *loc. cit.*) and from a comparison of its physical properties with those of the *cis*-isomer described below. Quantitative spectrometric measurements, which will be reported in detail later, show that the rearrangement of *cis*-phenylpropenylcarbinol is about half as fast as that of the *trans*-isomer and that the product in each case contains less than 5% of methyl-*cis*-styrylcarbinol.

Ph·CH(OH)·CH=CHMe	Ph·CH=CH·CHMe·OH	Ph·C≡C·CHMe·OH
(I; *a* = *cis*; *b* = *trans*.)	(II; *a* = *cis*; *b* = *trans*.)	(III.)

To confirm the configuration of (II*b*) and test the possibility that its formation as above might proceed partly or wholly through (II*a*), the latter was synthesized by condensing phenylethynylmagnesium bromide with acetaldehyde and partially hydrogenating the resulting 4-phenylbut-3-yn-2-ol (III) in the presence of a palladium–calcium carbonate catalyst. *cis*-Methylstyrylcarbinol (II*a*), unlike the *trans*-isomer, is a liquid at room temperature and there are interesting differences in their light absorption properties. The infra-red results which were

kindly determined by Mr. Philpotts and Mr. Thain (cf. *Nature*, 1950, **166**, 1028) are shown in Fig. 1. As with the stereoisomeric phenylpropenylcarbinols (Braude and Coles, *loc. cit.*), the *trans*-isomer exhibits bands near 970 and 760 cm.$^{-1}$ which are much more intense than those of the *cis*-isomer. The assignment of the 760-cm.$^{-1}$ band is uncertain, while the 970-cm.$^{-1}$ band also appears in other *trans*-ethylenic carbinols and is ascribed to superposed deformation frequencies of the –C–O–H and R–CH=CH–R groupings; it is noteworthy that this frequency is very little affected by conjugation with a phenyl group.

The ultra-violet data are shown in Fig. 2. Both methylstyrylcarbinols exhibit an intense band near 2500 A. associated with the styryl chromophore, but whereas the maximum of the *trans*-

FIG. 2.

Ultra-violet light absorption of methyl-cis- (· — · — · —) *and* -trans-*styrylcarbinol* (————) *in ethanol.*

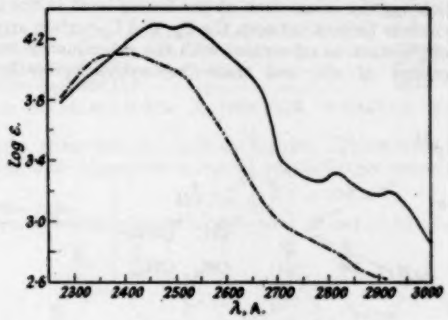
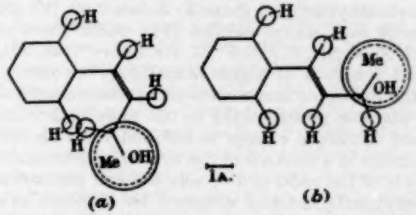


FIG. 3.

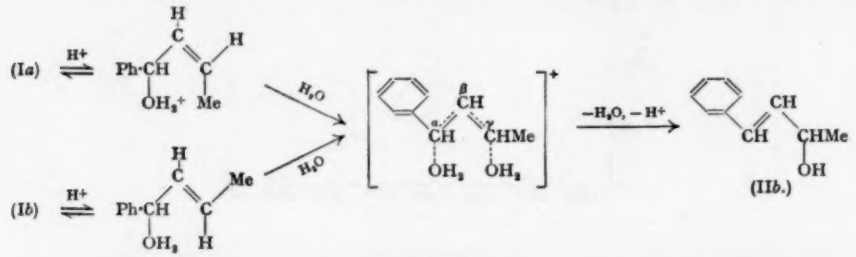
Planar projections (covalent bond radii) of methyl-cis-*styrylcarbinol* (*a*) *and* trans-*methylstyryl-carbinol* (*b*).



isomer (2510 A., ε 19,500) is displaced towards longer wave-lengths and intensified with respect to that of styrene itself ($\lambda_{max.}$ 2420 A., ε 10,000), the location and intensity of the maximum of the *cis*-isomer (2400 A., ε 12,000) are very similar to those of styrene. It has previously been shown (Braude and Timmons, *J.*, 1950, 2000) that the bathochromic and hyperchromic displacements of the *K*-band in the *trans*-isomer is due to the hyperconjugative effect of the CHMe·OH substituent, *e.g.*, to contributions from $+$ $=CH-CH=CHMe\ OH^-$. Now, hyperconjugation like other types of conjugation imparts some double-bond character to conventional single bonds and therefore requires a coplanar or nearly coplanar arrangement of the groups concerned. In methyl-*trans*-styrylcarbinol, there is no hindrance to free rotation of the CHMe·OH group, but in the *cis*-isomer (Fig. 3) considerable steric interference occurs with the *o*-hydrogen atoms of the phenyl group (Fig. 3 has been drawn with covalent radii which represent a *minimum* measure of interference; cf., *J.*, 1949, 1890). Consequently, hyperconjugation will be inhibited, with the result that the absorption closely resembles that of styrene itself. A similar case of steric inhibition of hyperconjugation has been observed in the more highly substituted dimethyl-α-methyl-*trans*-styrylcarbinol (Braude and Timmons, *loc. cit.*).

Methyl-*cis*-styrylcarbinol shows no tendency to isomerise to the *trans*-isomer under ordinary conditions or in presence of dilute acids in aqueous dioxan. It may therefore be concluded that methyl-*trans*-styrylcarbinol is the *direct* product of the oxotropic rearrangement of both *cis*- and *trans*-phenylpropenylcarbinol. This result is not unexpected. It has been shown that, under the conditions used, the reaction proceeds predominantly by way of a bimolecular attack of a solvent water molecule at the γ-carbon atom of the oxonium ion, formed by the reversible addition of a proton to the hydroxyl group of the carbinol (Braude, Jones, and Stern, *loc. cit.*; Braude, *Ann. Reports*, 1949, **46**, 125; *Quart. Reviews*, 1950, **4**, 404). Initially, rotation about the C_α–C_β bond will be quite free, but during the formation of the transition state the phenyl group would be expected to take up a position on the far rather than on the near side of the γ-carbon atom, since the latter arrangement would result in serious over-crowding which is shown by scale models and borne out by the physical properties of methyl-*cis*-styrylcarbinol (see below). Thus, whichever the orientation of the double bond in the unrearranged carbinol, the new double bond which is formed between the C_α- and C_β-carbon atoms would be expected to assume the *trans*-configuration, in agreement with the experimental results in this case.

Oxotropic Rearrangement of cis- *and* trans-*Propenylvinylcarbinols.*—The acid-catalysed



rearrangement of *trans*-propenylvinylcarbinol (*trans*-hexa-1 : 4-dien-3-ol) (IV*b*) was first studied by Heilbron, Jones, McCombie, and Weedon (*loc. cit.*) who found that under mild conditions the only product is butadienylmethylcarbinol (hexa-3 : 5-dien-2-ol) (V) although the latter undergoes further rearrangement into sorbyl alcohol (VI) under more strongly acid conditions (Nazarov and Fisher, *Bull. Acad. Sci. U.R.S.S., Cl. Sci. Chim.*, 1948, **311**, 427). A more detailed study of the corresponding reactions of higher homologues has shown (Braude and Timmons, *J.*, 1950, 2007) that in the oxotropic rearrangement of unsymmetrical dialkenylcarbinols, the hydroxyl group always migrates preferentially to the more highly substituted γ-carbon atom and that the three-carbon oxotropic change is followed by a slower, reversible, five-carbon oxotropic change which results in a mixture of the two conjugated isomers. As the ratio of the rates of the two reactions is of the order of 10^3, only the first product is isolated under suitable conditions. The butadienylmethylcarbinol obtained by Heilbron *et al.* (*loc. cit.*) formed an α-naphthylurethane, m. p. 84°; it gave a maleic anhydride adduct readily and in good yield and therefore consisted mainly, or entirely, of the *trans*-isomer (V*b*). *cis*-Propenylvinylcarbinol (Braude and Coles, *loc. cit.*) similarly rearranges in the presence of dilute mineral acid to a butadienylmethylcarbinol, the skeletal structure of which was proved by catalytic hydrogenation to hexan-2-ol and oxidation of the latter to *n*-butyl methyl ketone, identified as the 2 : 4-dinitrophenylhydrazone. The rearrangement is about half as fast as that of the *trans*-

Me·CH=CH·CH(OH)·CH=CH_2 (IV; *a* = *cis*; *b* = *trans*.)

Me·CH(OH)·CH=CH·CH=CH_2 (V; a = *cis*; b = *trans*.)

Me·CH=CH·CH=CH·CH_2·OH (VI.)

Me·CH=CH·CH=CH_2 (VII.)

isomer, and, as in the latter case, no detectable amount of the alternative rearrangement product, sorbyl alcohol (VI), is formed under these conditions. However, unlike the *trans*-butadienylmethylcarbinol obtained from *trans*-propenylvinylcarbinol, the butadienylmethylcarbinol produced by rearrangement of *cis*-propenylvinylcarbinol gave an α-naphthylurethane, m. p. 74—75°, and did not form a maleic anhydride adduct and must therefore be *cis*-butadienylmethylcarbinol (V*a*). The stereochemical relations of the geometrical isomers are reflected in a regularity of the melting points of the α-naphthylurethanes (Table I).

TABLE I.

M. p.s of α-naphthylurethanes.

	cis-Isomer.	*trans*-Isomer.	Difference.
Propenylvinylcarbinols (IV)	86—88°	94—95°	7—8°
Butadienylmethylcarbinols (V)	74—75	85—86	11

The two stereoisomeric butadienylmethylcarbinols also exhibit an interesting difference in ultra-violet light absorption. Both have a maximum at the same wavelength as piperylene (VII), but that of the *trans*-isomer is somewhat intensified, whereas that of the *cis*-isomer is somewhat reduced in intensity. By contrast, *cis*- and *trans*-piperylene have maxima of identical intensity in ethanol solution (Table II).*

TABLE II.

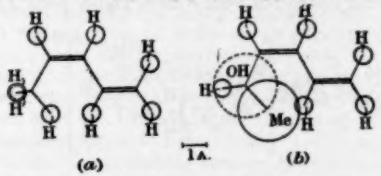
	$\lambda_{max.}$, A.	$\varepsilon_{max.}$ (in ethanol).
cis-Piperylene (VII*a*)	2230	22,600
trans-Piperylene (VII*b*)	2235	23,000 [1]
cis-Butadienylmethylcarbinol (V*a*)	2240	20,000
trans-Butadienylmethylcarbinol (V*b*)	2230	28,000 [2]

[1] Booker, Evans, and Gillam, *J.*, 1940, 1453. [2] Heilbron, *et al.*, *loc. cit.*

Our interpretation of these data is briefly as follows. The enhanced intensity in the *trans*-carbinol (V*b*) compared with piperylene is caused by the larger hyperconjugative effect of the

FIG. 4.

Planar projections (covalent bond radii) of cis-*piperylene* (*a*) *and* cis-*butadienylmethylcarbinol* (*b*).



(*a*) (*b*)

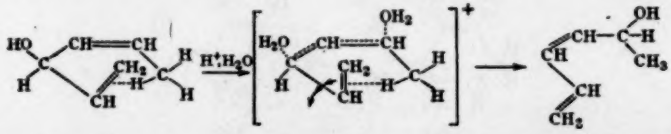
–C–OH compared with the –C–H grouping; similar differences are found for other ethylenic carbinols (Braude and Timmons, *J.*, 1950, 2000, 2007). The reduced intensity in the *cis*-carbinol (V*a*) is ascribed to steric interference between the CHMe·OH and the $CH{=}CH_2$ groupings (see Fig. 4*b*) which prevents complete coplanarity of the hyperconjugated system; this effect is very similar to, but smaller than, that observed for methyl-*cis*-styrylcarbinol (see above).† In piperylene, on the other hand, no steric opposition to coplanarity is indicated in the *cis*-form (see Fig. 4*a*) and the absorption of the two geometrical isomers is therefore identical.

The formation of the two different stereoisomeric butadienylmethylcarbinols by the rearrangement of *cis*- and *trans*-propenylvinylcarbinols is quite unexpected, for two reasons. First, whatever the relative stability of the *cis*- and *trans*-butadienylmethylcarbinols, *the same*

* In heptane, the value of $\varepsilon_{max.}$ is about 10% higher for *trans*- than for *cis*-piperylene (Jacobs and Platt, *J. Chem. Physics*, 1948, **76**, 1142). In this less solvating solvent, the vibrational structure of the bands is more pronounced and the shapes of the band-envelopes for the two isomers differ considerably. In such circumstances, the integrated band areas rather than $\varepsilon_{max.}$ must be used as a measure of the probability of the electronic transition and are, in fact, identical within experimental error. In the vapour phase, the value of $\varepsilon_{max.}$ for *trans*-piperylene is reported to be almost doubled (Jacobs and Platt, *loc. cit.*). The reason for this is not clear.

† There is a significant difference between the two cases. The main contribution to hyperconjugation comes from the C–OH bond and for this hyperconjugation to be fully effective, the C–OH bond must be parallel to the π-electron orbitals of the styryl system, *i.e.*, *at right angles* to the plane of the styryl system. This requirement follows both from valency-bond theory, since the other three groups attached to the terminal carbon atom will tend to be coplanar in the extreme hyperconjugated structure $X^- {=}CH{-}CH{=}CR_2\,OH^+$, and from molecular-orbital theory by the principle of maximum overlap. In the optimum arrangement, the C–H and C–Me bonds of the CHMe·OH group will therefore be symmetrically disposed at angles of about 18° with respect to the plane of the styryl system. Now with *cis*-methylstyrylcarbinol, steric interference is indicated for either of the two rotational positions of the CHMe·OH group, representing the optimum arrangement. With *cis*-butadienylmethylcarbinol, on the other hand, steric interference is indicated in only one (*e.g.*, that shown in Fig. 4*b*) of the two rotational positions representing the optimum arrangement of the CHMe·OH group. Thus steric inhibition of hyperconjugation will be less severe in the latter case. These matters will be dealt with more fully in a forthcoming publication in another series (cf. *J.*, 1949, 1890).

product would be expected from both cis- *and* trans-*propenylvinylcarbinols since rotation about the* C_α–C_β *bond should be essentially free,* so that the configuration of the rearranged carbinol should be independent of the configuration of the starting carbinol. Secondly, it would be expected that the rearranged *trans*-carbinol should be formed preferentially, as in the case of methylstyrylcarbinol, since in the rearranged *cis*-carbinol effective conjugation is somewhat inhibited by steric hindrance to coplanarity. However, one of these assumptions is evidently incorrect, and some factor is clearly operative which results in the formation of the thermodynamically less stable structure from *cis*-propenylvinylcarbinol. The conclusion appears inevitable that rotation about the C_α–C_β bond is essentially free in *trans*-propenylvinylcarbinol, but not free in *cis*-propenylvinylcarbinol and that *some interaction occurs between the* cis-*methyl substituent and the vinyl group, which holds the latter in a* cis-*orientation both before and during the rearrangement.* In explanation, we advance the tentative hypothesis that this effect has its origin in the hyperconjugation of the propenyl group which confers a fractional positive charge on the hydrogen atoms of the *cis*-methyl substituent and that an intramolecular interaction takes place between the hyperconjugated hydrogen atoms and the π-electrons of vinyl group to form a pseudo-cyclic structure, as shown below (IV*a*). Such an interaction, which may be termed "π-hydrogen bonding," can be visualised as intermediate in character between ordinary hydrogen bonding, in which a potential proton interacts with a basic group, such as NR_2 or OR, carrying unshared electron pairs, and π-bonding, in which a cation or potential cation, such as H^+, Ag^+ or Br^+, interacts with the unsaturation electrons of a multiple bond (Dewar, *J.*, 1946, 406; for further examples, see Hildebrand, Benesi, and Mower, *J. Amer. Chem. Soc.*, 1950, **72**, 1017; Mulliken, *ibid.*, p. 600; Andrews and Keefer, *ibid.*, pp. 5034, 5170; Brown *et al.*, *ibid.*, p. 5347). The present conception is novel, however, in that the π-bonded proton is derived from a hyperconjugated C–H bond, instead of from a more highly polar N–H, O–H, or Hal–H bond.



π-Hydrogen bonding must be visualised as a weak type of bonding, representing a stabilisation of not more than 1—2 kcals./mole. This is clearly shown by the fact that *cis*-phenylpropenylcarbinol, in which π-hydrogen bonding would similarly be expected to take place between the *cis*-methyl and the phenyl group, rearranges to the *trans*-styryl isomer. In this case, any stabilisation of the *cis*-orientation in the unrearranged carbinol is clearly outweighed by steric opposition to the formation of the *cis*-rearranged isomer, which may amount to not less than 4 kcals./mole and becomes the controlling factor in the transition state, as was discussed above (p. 2088). Again, *iso*butenylvinylcarbinol (VIII), which contains both a *cis*- and a *trans*-methyl substituent, appears to rearrange to *trans*-butadienyldimethylcarbinol (IX*b*) since the product

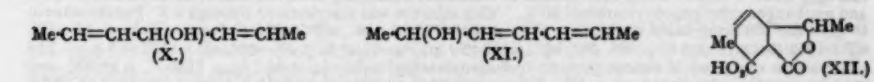
$Me_2C{=}CH{\cdot}CH(OH){\cdot}CH{=}CH_2$ (VIII.) $\qquad$ $Me_2C(OH){\cdot}CH{=}CH{\cdot}CH{=}CH_2$ (IX.)

gives a maleic anhydride adduct in moderate yield and has normal light-absorption properties (Braude and Timmons, *locc. cit.*). In this case also, the corresponding *cis*-rearranged isomer will be considerably more sterically hindered than *cis*-butadienylmethylcarbinol; in addition π-hydrogen bonding will be weaker in (VIII) than in (IV*a*), since reactivity data show that the extent of hyperconjugation *per methyl substituent* is considerably smaller in an *iso*butenyl than in a propenyl group (Braude and Jones, *J.*, 1946, 122, 128).

The observation that the oxotropy of two stereoisomeric ethylenic carbinols can give rise to two different stereoisomeric products has another important consequence, which is quite independent of the above explanation. Although recent work from this laboratory has provided strong evidence for a mechanism of oxotropy which involves bimolecular attack by a neutral reagent at the γ-carbon atom of the oxonium ion (cf. Braude, *Ann. Reports*, 1949, **46**, 125; Braude and Forbes, *J.*, 1951, 1755), yet it has not been possible hitherto to exclude with certainty an alternative view, which involves unimolecular ionisation of the oxonium ion into a free mesomeric carbonium ion. Indeed, the exponents of the latter type of mechanism (cf. Catchpole, Hughes, and Ingold, *J.*, 1948, 8) still consider that the carbonium ion may be formed by direct ionisation of the carbinol, whereas we have for some time regarded the preceding formation of

the oxonium ion and the essential requirement of hydrogen-ion catalysis in aqueous media as definitely proven. *The present results, moreover, provide compelling evidence against the intervention of the free, mesomeric carbonium ion,* for the following reason. The postulate of a free carbonium-ion intermediate is equivalent to the assumption of a reversible heterolysis of the existing C–O bond *before* the new C–O bond is formed, and to a reversible migration of the fully developed positive charge from one end to the other of the pentadiene chain. Under such conditions, the stereochemical configuration about each of the carbon bonds will be quite labile and the hypothetical ions derived from two stereoisomeric carbinols such as (IV*a*) and (IV*b*) would be able to adopt the same configuration or mixture of configurations, and therefore give rise to sterically identical products.

Oxotropic Rearrangement of cis-trans-*Dipropenylcarbinol.*—*cis-trans*-Dipropenylcarbinol (-hepta-2 : 5-dien-4-ol) (X*a*), like its lower homologue, undergoes oxotropic rearrangement in the presence of dilute acids to give the conjugated isomer hepta-3 : 5-dien-2-ol (XI). The skeletal structure of the product was proved by its ultra-violet light absorption ($\lambda_{max.}$ 2270 A., ε 23,000), typical of a diene system containing two alkyl substituents, and by catalytic hydrogenation to heptan-2-ol, followed by oxidation to *n*-amyl methyl ketone, identified as the 2 : 4-dinitrophenylhydrazone. Although (X) is skeletally symmetrical and can give rise to



only one type of conjugated isomer, an element of dissymmetry is introduced in the present instance through the different geometrical configurations of the propenyl groups and the rearrangement can involve the migration of either of the ethylenic bonds. As judged by the results obtained in the oxotropy of the propenylvinylcarbinols, the new double bond formed would be expected to have a different geometrical configuration in the two cases. Since, moreover, the rates of rearrangement of *cis-* and *trans*-propenylvinylcarbinol are of the same order, it would be expected that the rearrangement of *cis-trans*-dipropenylcarbinol will give rise to a mixture of stereoisomeric hepta-3 : 5-dien-2-ols. This is in accord with the extinction coefficient of the product, which is intermediate between the values for a *cis-* and a *trans*-dienol (Table II) and with the fact that the product reacted with maleic anhydride to give a low yield of adduct which was isolated as the lactonic acid (XII) analogous to those obtained from homologous dienols (Heilbron *et al., loc. cit.*; Braude and Timmons, *loc. cit.*). Although the possibility of some geometrical isomerisation under the influence of the reagents cannot definitely be excluded, it thus appears that the rearrangement of *cis-trans*-dipropenylcarbinol yields a mixture of the *cis-trans-* and *trans-trans*-isomers (XI).

Experimental.

M. p.s were determined on a Kofler block and are corrected.

*Rearrangement of Phenyl-*cis-*propenylcarbinol* (I*a*).—A solution of phenyl-*cis*-propenylcarbinol (Braude and Coles, *loc. cit.*, p. 2082; 9 g.) in 60% aqueous acetone (100 ml.) 0·01M. in respect of hydrochloric acid was kept for 20 hours at room temperature. After neutralisation with sodium carbonate, the acetone was distilled off and the residue extracted with ether. Fractionation of the ethereal extract from a trace of potassium carbonate gave methyl-*trans*-styrylcarbinol (6 g.), b. p. 97°/0·1 mm., n_D^{19} 1·5654 (Braude, Jones, and Stern, *J.*, 1946, 396, give b. p. 104°/1 mm., n_D^{21} 1·5665), the ultra-violet and infra-red light absorptions of which were indistinguishable from those (Figs. 1*a* and 1*b*) of an authentic specimen obtained by the rearrangement of phenyl-*trans*-propenylcarbinol. It formed a *p*-nitrobenzoate, m. p. 57—58° (Kenyon, Partridge, and Phillips, *J.*, 1937, 207, give m. p. 58—59°), undepressed on admixture with an authentic specimen.

4-*Phenylbut-*3-*yn-*2-*ol* (III) *and Methyl-*cis-*styrylcarbinol* (II*a*).—Phenylacetylene (34 g.) (Nef, *Annalen*, 1899, **308**, 267), b. p. 95°/166 mm., n_D^{24} 1·5468, in ether (30 ml.) was gradually added to a solution of ethylmagnesium bromide (from Mg, 9 g.) in ether (300 ml.) (cf. Wilson and Hyslop, *J.*, 1924, 1556). After 4 hours' refluxing, the solution was cooled to 0° and freshly distilled acetaldehyde (16 g.) in ether (30 ml.) was added. Stirring was continued overnight and the products were then worked up in the usual manner to give 4-*phenylbut-*3-*yn-*2-*ol* (30 g., 61%), b. p. 101°/0·3 mm., n_D^{21} 1·5672 (Found: C, 82·5; H, 7·1. $C_{10}H_{10}O$ requires C, 82·2; H, 6·9%).

4-Phenylbut-3-yn-2-ol (4·85 g., 0·033 mol.) in methanol (25 ml.) was hydrogenated in the presence of 0·3% palladium–calcium carbonate (0·4 g.) until 800 ml. (0·033 mol.) at 20°/766 mm. had been absorbed. Removal of the catalyst and fractionation gave methyl-*cis*-styrylcarbinol (3·6 g.), b. p. 77°/0·1 mm., n_D^{21} 1·5510 (Found: C, 80·95; H, 8·1. $C_{10}H_{12}O$ requires C, 80·9; H, 8·1%). Light absorption: see Figs. 1*a* and 1*b*. The ultra-violet light absorption of a solution of the carbinol in 60% aqueous dioxan 0·1M. in respect of hydrochloric acid remained unchanged after 18 hours at room temperature.

Rearrangement of cis-*Propenylvinylcarbinol* (IV*a*).—(*a*) A solution of *cis*-propenylvinylcarbinol prepared by the condensation of *cis*-propenyl-lithium with acraldehyde (Braude and Coles, *loc. cit.*, p. 2083) (4 g.) in 60% aqueous acetone (100 ml.) 0·05M. in respect of hydrochloric acid was kept at room temperature for 20 hours. After neutralisation with sodium carbonate (0·3 g.), the acetone was distilled off through an 8″ Fenske column, and the residue extracted with ether. Fractionation of the ethereal extract gave cis-*butadienylmethylcarbinol* (cis-*hexa*-3 : 5-*dien*-2-*ol*) (2 g.), b. p. 113°/99 mm., 57—58°/14 mm., n_D^{21} 1·4800 (Found: C, 73·6; H, 10·0. $C_6H_{10}O$ requires C, 73·4; H, 10·25%). Light absorption in ethanol: Max. at 2240 A., ε 20,000. The carbinol formed an α-naphthylurethane, m. p. 74—75° (Found: C, 76·6; H, 6·4. $C_{17}H_{17}O_2N$ requires C, 76·4; H, 6·4%), but gave no adduct on being kept with maleic anhydride in benzene for a week.

Hydrogenation of *cis*-butadienylmethylcarbinol (0·6 g.) in methanol (20 ml.) in the presence of platinic oxide resulted in the uptake of 320 ml. at 20°/763 mm. (Calc., 300 ml.). After removal of the catalyst and solvent, the residue was taken up in ether (10 ml.) and oxidised by shaking it with potassium dichromate (0·7 g.) in M-sulphuric acid. The product was extracted with ether and converted into the 2 : 4-dinitrophenylhydrazone. Chromatography of the latter on alumina from benzene solution yielded only the *n*-butyl methyl ketone derivative, which after crystallisation from aqueous methanol had m. p. 108°, undepressed on admixture with an authentic specimen.

(*b*) A mixture (2 g.; b. p. 44—47°/12 mm., n_D^{20} 1·4500) of *cis*-propenylvinylcarbinol and ethylpropenylcarbinol, obtained by partial hydrogenation of ethynylpropynylcarbinol (Braude and Coles, *loc. cit.*) was treated with aqueous acetone and hydrochloric acid as under (*a*). The product before fractionation had $\lambda_{max.}$ 2240, ε 10,200 which corresponds to a mixture consisting of *cis*-butadienylmethylcarbinol 50% and unchanged ethylpropenylcarbinol 50%. This mixture was fractionated through a 3″ Fenski column to give the following main fractions: (i) b. p. 56—57°/15 mm., n_D^{24} 1·4615 (0·5 g.); (ii) b. p. 57—58°, n_D^{24} 1·4652 (0·4 g.); (iii) b. p. 58—59°, n_D^{24} 1·4696 (0·4 g.); and (iv) b. p. 59—60°, n_D^{24} 1·4738 (0·3 g.). The last fraction consisted of almost pure *cis*-butadienylmethylcarbinol; it had $\lambda_{max.}$ 2240 A., ε 19,500, and gave an α-naphthylurethane, m. p. 75—76°, undepressed on admixture with specimen obtained as under (*a*), but depressed to 67—69° on admixture with the α-naphthylurethane of ethylpropenylcarbinol (Braude and Coles, *loc. cit.*, p. 2084).

Rearrangement of cis-trans-*Dipropenylcarbinol* (X).—A solution of *cis-trans*-dipropenylcarbinol (Braude and Coles, *loc. cit.*, p. 2084) (6 g.) in 60% aqueous acetone (100 ml.) 0·01M. in respect of hydrochloric acid was kept for 1 hour at room temperature. After neutralisation with potassium carbonate (70 mg.) the acetone was distilled off through an 8″ Fenske column, the aqueous residue was extracted with ether, and the ethereal extract was dried (Na_2SO_4–K_2CO_3) and fractionated to give *hepta*-3 : 5-*dien*-2-*ol* (4·5 g.), b. p. 78°/20 mm., n_D^{21} 1·4897 (Found: C, 74·7; H, 10·8. $C_7H_{12}O$ requires C, 75·0; H, 10·8%). Light absorption in ethanol: $\lambda_{max.}$ 2270 A., ε 20,700. A solution of the carbinol (0·5 g.) and maleic anhydride (0·5 g.) in dry benzene (2 ml.), after being kept for 2 weeks, deposited 3-1′-*hydroxyethyl*-6-*methyl*cyclo*hexene*-4 : 5-*dicarboxylic acid* 4-*lactone* (XII) (0·2 g.) which crystallised from aqueous ethanol in prisms, m. p. 182—183° (Found: C, 62·7; H, 6·8. $C_{11}H_{14}O_4$ requires C, 62·85; H, 6·7%).

Hydrogenation of hepta-3 : 5-dien-2-ol (1·95 g.) in methanol (30 ml.) in the presence of platinic oxide resulted in the uptake of 820 ml. at 18°/768 mm. (Calc., 825 ml.) to give *n*-heptan-2-ol (1·6 g.). A small portion was converted into the α-naphthylurethane which was crystallised from light petroleum (b. p. 100—120°) and had m. p. 122—123°. The remainder (1·5 g.) was dissolved in ether (10 ml.) and oxidised with potassium dichromate (1·3 g.) in M-sulphuric acid (30 ml.), to give *n*-amyl methyl ketone, identified as the 2 : 4-dinitrophenylhydrazone (2·1 g.) which after chromatography on alumina from benzene solution and crystallisation from methanol had m. p. 96—97°, undepressed on admixture with an authentic specimen.

cis-*Piperylene*.—A sample of highly purified *cis*-piperylene, b. p. 43·2°/733 mm., n_D^{20} 1·4360, was kindly furnished by Dr. D. Craig, to whom we express our thanks.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
SOUTH KENSINGTON, LONDON, S.W.7.

[*Received, February 9th*, 1951.]

463. *Studies in Molecular Rearrangement. Part VIII.* The Five-carbon Oxotropic Rearrangement of 1-Phenylhexa-2 : 4-dien-1-ol.*

By H. C. Barany, E. A. Braude, and J. A. Coles.

The reaction of sorbaldehyde with phenylmagnesium bromide gives 1-phenylhexa-2 : 4-dien-1-ol (VI) which undergoes five-carbon oxotropy under acidic conditions to 6-phenylhexa-3 : 5-dien-2-ol (VII). The latter has been dehydrated to 1-phenylhexa-1 : 3 : 5-triene (IX).

Kinetic measurements for the rearrangement are reported and discussed. It is shown that the partly rearranged isomer, 1-phenylhexa-1 : 4-dien-3-ol (VIII), is not an intermediate, and the reaction is considered to proceed mainly by way of a bimolecular attack by a water molecule at the $C_{(5)}$-atom of the oxonium ion (X). The mobility of the system (VI) ⟶ (VII) is compared with that of the corresponding three-carbon rearrangement of 1-phenylbut-2-en-1-ol (XI) to 4-phenylbut-3-en-2-ol (XII).

Whereas three-carbon anionotropy has been known for many years and has been extensively investigated (for a summary, cf. Braude, *Quart. Reviews*, 1950, **4**, 404), five-carbon anionotropic systems have been little studied until quite recently. The first example of an open-chain oxotropic system was provided by Heilbron, Jones, and McCombie (*J.*, 1944, 134), who condensed sorbaldehyde with sodium acetylide and showed that the resulting carbinol (I; X = C:CH, R = Me) readily underwent rearrangement to the fully conjugated isomer (II; X = C:CH, R = Me), in the presence of dilute acids. A number of similar examples have since been

(I.) HO·CHX·CH:CH·CH:CHR CHX:CH·CH:CH·CHR·OH (II.)

described (Heilbron *et al.*, *J.*, 1949, 287, 742, 2023) and it has been shown that butadienylcarbinols carrying only alkyl substituents (*e.g.* I; X = H, R = Me) undergo reversible five-carbon oxotropy, leading to a mixture of the two isomers (Nazarov and Fisher, *Bull. Acad. Sci., U.R.S.S., Cl. Sci. Chim.*, 1945, 631; 1948, 311, 427; Braude and Timmons, *J.*, 1950, 2007).

The Synthesis, Rearrangement, and Dehydration of 1-*Phenylhexa*-2 : 4-*dien*-1-*ol.*—The present work originally had the twofold object of (*a*) providing an example of five-carbon oxotropy in a system terminated by a phenyl group, and (*b*) carrying out a quantitative comparison of mobility in three- and five-carbon oxotropic systems. In the meantime, however, Woods and Sanders (*J. Amer. Chem. Soc.*, 1947, **69**, 2926) have described the isomerisation of 1-phenylpenta-2 : 4-dien-1-ol (III) to 5-phenylpenta-2 : 4-dien-1-ol (IV), and the rearrangement of the corresponding

(III.) HO·CHPh·CH:CH·CH:CH_2 CHPh:CH·CH:CH·CH_2·OH (IV.)

(V.) CHPh:CH·CH(OH)·CH:CH_2

tertiary homologue, 2-phenylhexa-3 : 5-dien-2-ol, has recently been investigated by Nazarov and Fisher (*Bull. Acad. Sci., U.R.S.S.*, 1949, 386). We chose for study 1-phenylhexa-2 : 4-dien-1-ol (VI) which was readily prepared by the reaction of sorbaldehyde with phenylmagnesium bromide; its constitution was confirmed by its ultra-violet light absorption properties and by catalytic hydrogenation which resulted in the uptake of 2 molecular equivalents of hydrogen giving 1-phenylhexan-1-ol. In the presence of dilute hydrochloric acid in aqueous acetone or dioxan solution, 1-phenylhexa-2 : 4-dien-1-ol underwent rearrangement to the fully conjugated, isomeric 6-phenylhexa-3 : 5-dien-2-ol (VII), which exhibited ultra-violet light absorption characteristic of the phenylbutadiene system (see figure). Quantitative measurements (see below)

(VI.) HO·CHPh·CH:CH·CH:CHMe CHPh:CH·CH:CH·CHMe·OH (VII.)

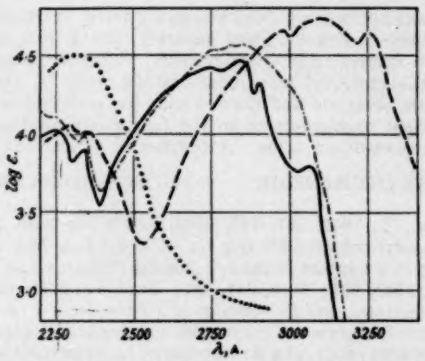
(VIII.) CHPh:CH·CH(OH)·CH:CHMe CHPh:CH·CH:CH·CH:CH_2 (IX.)

show that rearrangement is substantially complete. In contrast to the other two homologous systems previously investigated, both isomers were obtained as solids at room temperature.

The isomerisation of (III) to (IV) and (VI) to (VII) could conceivably proceed by two

* Part VII, preceding paper.

successive 3-carbon oxotropic rearrangements, *via* the intermediates (V) and (VIII), respectively. This possibility was first considered by Salkind and Kulikov (*J. Gen. Chem., U.S.S.R.*, 1945, **15**, 643) who obtained what they concluded to be a mixture of (III), (IV), and (V), with the latter predominating, by partial hydrogenation of 1-phenylpent-2-en-4-yn-1-ol in ethyl acetate. No rearrangement would normally be expected under these conditions, and it must be presumed that any isomerisation which did occur was due to acetic acid impurities in the solvent. However, the evidence for the constitution of the dienol mixture obtained by Salkind and Kulikov is in any case by no means conclusive, and the formation of (V) was not observed by Woods and Sanders (*loc. cit.*). Similarly, no trace of 1-phenylhexa-1 : 5-dien-3-ol (VIII) was isolated in the present work from the rearrangement of 1-phenylhexa-2 : 4-dien-1-ol (VI). This, of course, does not necessarily exclude the possible formation of (VIII) as an intermediate, but the fact that no appreciable concentration of (VIII) is ever present during the rearrangement of (VI) to (VII) was readily established by following the reaction spectrometrically. The carbinol (VIII) contains the styrene chromophore and can safely be predicted to exhibit intense light-absorption maximum near 2510A. ($\varepsilon \sim 20{,}000$) similar to that of cinnamyl alcohol and its homologues (Braude, Jones, and Stern, *J.*, 1946, 396; Braude and Timmons, *loc. cit.*), whereas the carbinols (VI) and (VII) exhibit only relatively low-intensity absorption ($\varepsilon \sim 2000$) in this region (see figure).



Ultra-violet light absorption of 1-*phenylbutadiene* (——), 1-*phenylhexa*-2 : 4-*dien*-1-*ol* (· · · · · · ·), 1-*phenylhexa*-1 : 3-*dien*-5-*ol* (— · — · —) *and* 1-*phenylhexatriene* (– – – – –) *in ethanol solution.*

Quantitative measurements (see Experimental) show that the intensity of absorption at 2510A. throughout the rearrangement remains equal, within experimental error, to that expected for the appropriate mixture of (VI) and (VII) alone, and that the possible concentration of (VIII) at any time must be less than 1% of the concentration of (VII). Further evidence, which also excludes the incursion of (VIII) as an " unstable " intermediate, is provided by kinetic measurements which are discussed below.

On distillation from potassium hydrogen sulphate under carefully controlled conditions, 1-phenylhexa-2 : 4-dien-1-ol underwent simultaneous rearrangement and dehydration to 1-phenylhexa-1 : 3 : 5-triene (IX), which has not previously been described. It was obtained as a low-melting solid and exhibited the expected light-absorption properties (see figure) with a high-intensity maximum near 3110 A. showing some vibrational structure.

The Kinetics and Mechanism of the Rearrangement of 1-*Phenylhexa*-2 : 4-*dien*-1-*ol.*—The kinetics of the rearrangement of (VI) to (VII) under standard conditions employed in earlier studies on three-carbon oxotropy have been determined by the spectrometric technique, use being made of the change in absorption intensity at 2810 A. where (VII) exhibits a maximum. The reaction is strictly of the first order in dilute hydrochloric acid in aqueous dioxan solution (see Experimental). Rate constants were determined for two solvent compositions at 5° intervals in the temperature range 30—50°; they gave linear Arrhenius plots. As usual, the rates of rearrangement are higher, and the Arrhenius energies of activation lower, in 40% than in 60% aqueous dioxan. The results are summarised in Tables I and II, together with those for the rearrangement of phenylpropenylcarbinol (XI) to methylstyrylcarbinol (XII) for comparison.

The five-carbon rearrangement is about ten times more rapid than the corresponding three-carbon rearrangement, and has a somewhat lower energy of activation.

TABLE I.

First-order rate constants (10^4 k, *min.*$^{-1}$) *for the rearrangement* (VI) ⟶ (VII) *in a* 0·001M-*solution of hydrochloric acid in aqueous dioxan.*

Temp.	30°	35°	40°	45°	50°
40% dioxan	673	1080	1620	2250	3590
60% dioxan	175	308	495	812	1250

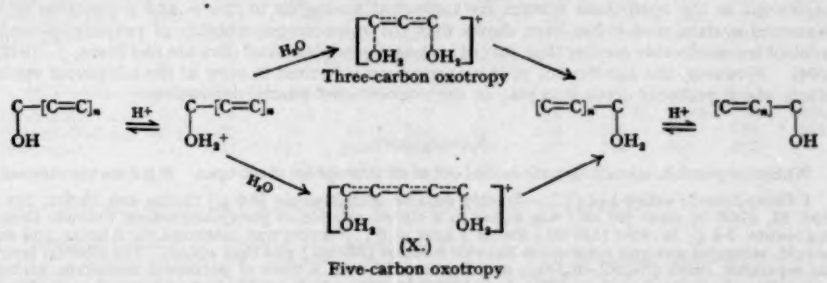
TABLE II.

Relative rate constants, energies of activation, and probability factors for three- and five-carbon oxotropic rearrangements in the system Ph·CH(OH)·$[CH{:}CH]_n$·Me.*

	40% dioxan.			60% dioxan.		
n.	k_{30}/c_A.	$E_{Arr.}$	log *A*.	k_{30}/c_A.	$E_{Arr.}$	log *A*.
1	7·2	18·2	12·2	1·84	19·5	12·6
2	67·3	16·1	11·7	17·5	19·0	13·1

* k_{30}/c_A is the first-order rate constant (min.$^{-1}$) at 30°, divided by the hydrochloric acid concentration. E_{Arr} and *A* are defined by the equation $\log k/c_A = Ae^{-E_{Arr}/RT}$, where E_{Arr} is expressed in kcal./mol. and *A* in sec.$^{-1}$.

Two aspects of these results call for comment; first, their bearing on the mechanism of five-carbon oxotropy, and second, the difference in mobility in the three- and the five-carbon oxotropic system. With regard to the first, there is no reason to expect, and there is no evidence to indicate, any difference in mechanism between acid-catalysed three-carbon and five-carbon oxotropy. The mechanism of three-carbon oxotropy has been exhaustively discussed (cf. Braude, *J.*, 1948, 794; *Ann. Reports*, 1949, **46**, 125), and it has been shown that in all the cases so far examined, the first step is a fast, reversible addition of a proton to the hydroxyl group to give the oxonium ion. In aqueous dioxan media, the reaction then proceeds mainly by way of a rate-determining bimolecular attack by a water molecule at the $C_{(3)}$-atom together with a small contribution, which increases with decreasing water content of the medium, from an intramolecular migration of a water molecule. The corresponding mode of reaction in five-carbon oxotropy will be bimolecular attack at the $C_{(5)}$-atom, as represented below.



The alternative possibility, that the five-carbon rearrangement takes place by two consecutive three-carbon rearrangements, is intrinsically unlikely on the basis of this mechanism, since the carbon-atom in the terminal, 5-position of the butadiene system in (VI) will be more highly polarised and more highly polarisable than in the intermediate 3-position, and will therefore be more highly susceptible to attack by a water molecule. It has already been shown that the partly rearranged isomer (VIII) is not an isolable intermediate, and evidence against its incursion as a non-isolable intermediate is afforded by the fact that the rearrangement of (VI) to (VII) accurately obeys the first-order rate law. It can be predicted from earlier studies on substituent effects (cf. Braude, *loc. cit.*) that if the two consecutive three-carbon rearrangements were involved, their rates could differ by a factor of less than 10, and it can easily be shown that a composite reaction of this type will not normally give rise to overall first-order kinetics.

The mechanism of five-carbon oxotropy has previously been discussed by Salkind and Kulikov (*loc. cit.*) and also by Dewar ("The Electronic Theory of Organic Chemistry," Oxford, 1949, p. 88). Salkind and Kulikov invoke a mechanism of the type first proposed by Burton and Ingold (*J.*, 1928, 904) involving ionisation of the carbinol into a carbonium ion and a hydroxyl ion, which does not, *inter alia*, account for the acid-catalysed nature of the reaction and does not merit further consideration. Dewar refers to the subject in the following words: "The mechanism is clearly similar to normal anionotropy of allyl compounds; the alcohol first forms a salt which then ionises to the mesomeric carbonium ion. This ion can combine with hydroxyl ion in a number of ways, but terminal addition is naturally favoured. . . . This mechanism has been supported by various kinetic measurements and certainly no other could account for migrations of hydroxyl from one end to the other of an extensive conjugated chain." It is necessary to comment, first, that as far as we are aware the present kinetic measurements are the first to be published on polycarbon oxotropy, and that the statement appears to refer mistakenly to previous investigations from this laboratory on three-carbon oxotropy; secondly, that any mechanism which invokes the participation of hydroxyl ions in a reaction which takes place relatively fast in acid solution and immeasurably slowly in neutral or alkaline solution must be viewed with mistrust; and thirdly, that the last part of the quoted statement is manifestly incorrect.

We now turn to the comparison of mobility in the five-carbon system (VI) ⟶ (VII) and the corresponding three-carbon system (XI) ⟶ (XII), which has previously been studied

(XI.) OH·CHPh·CH:CHMe CHPh:CH·CHMe·OH (XII.)

(Braude, Jones, and Stern, *J.*, 1946, 396; Braude and Stern, *J.*, 1947, 1096; 1948, 1982). Although the accuracy of the k values is of the order of $\pm 2\%$, that of E_{Arr} and log A is probably not better than $\pm 0{\cdot}3$ unit, and it is therefore justified to conclude from the data in Table II, that the enhanced mobility of the five-carbon system is largely due to a lower energy of activation, in conformity with previous results in this series (cf. Braude, 1950, *loc. cit.*). The lowering in energy of activation produced by the additional ethylenic grouping is not unexpected since there will be a higher degree of resonance stabilisation in the transition state (X) of the five-carbon than in the three-carbon system. The higher mobility may also be due partly to enhanced electron-accession at $C_{(1)}$. There is some evidence that the effect of a substituent (in this case, the hyperconjugative effect of the methyl group) increases with the length of the unsaturated system to which it is attached; thus the dissociation constant of sorbic acid ($k = 1{\cdot}73 \times 10^{-5}$) is smaller than that of crotonic acid ($k = 2{\cdot}03 \times 10^{-5}$). Again the 3- and 5-positions in the open-chain system are somewhat analogous to the *o*- and *p*-positions in a benzenoid system, and it has been shown that the anionotropic mobility of propenyl-*p*-tolylcarbinol is considerably greater than that of propenyl-*o*-tolylcarbinol (Braude and Stern, *J.*, 1947, 1096). However, the significance of this comparison is limited in view of the additional steric effects which probably come into play in the *o*-substituted phenyl derivatives.

Experimental.

Whenever possible, operations were carried out in an atmosphere of nitrogen. M.p.s are uncorrected.

1-*Phenylhexa*-2 : 4-*dien*-1-*ol* (VI).—Freshly distilled sorbaldehyde (9·6 g.) (Kuhn and Hoffer, *Ber.*, 1930, **63**, 2168) in ether (50 ml.) was added to a stirred solution of phenylmagnesium bromide (from magnesium, 2·4 g.) in ether (150 ml.) during 1 hour at 0°. Stirring was continued for 2 hours, and an ice-cold, saturated aqueous ammonium chloride solution (250 ml.) was then added. The ethereal layer was separated, dried (Na_2SO_4–K_2CO_3), and fractionated from a trace of potassium carbonate, giving 1-*phenylhexa*-2 : 4-*dien*-1-*ol* (9 g., 52%), b. p. 104°/0·05 mm., which solidified when kept; it crystallised from pentane in needles, m. p. 40—42° (Found: C, 83·0; H, 8·2. $C_{12}H_{14}O$ requires C, 82·9; H, 8·1%). Light absorption in ethanol: Maximum at 2310 A., ε 19,500.

Hydrogenation of 1-phenylhexa-2 : 4-dien-1-ol (3·7 g.) in ethanol (50 ml.) in the presence of platinic oxide (0·05 g.) resulted in the uptake of 950 ml. at 20°/761 mm. (Calc. 1000 ml.), and gave 1-phenylhexanol, b. p. 110—111°/1·5 mm. (Found: C, 81·2; H, 10·2. Calc. for $C_{12}H_{18}O$: C, 80·9; H, 10·1%) (Ipatieff and Haensel, *J. Amer. Chem. Soc.*, 1942, **64**, 521 give b. p. 128°/5 mm.). Light absorption in ethanol: Maximum at 2420 A. ε 60.

6-*Phenylhexa*-3 : 5-*dien*-2-*ol* (VII).—A solution of 1-phenylhexa-2 : 4-dien-1-ol (2·5 g.) in a 0·02M-solution (50 ml.) of hydrochloric acid in 60% aqueous acetone was kept for 20 hours at room temperature. The solution was then diluted with water neutralised with potassium carbonate, and extracted with ether. The ethereal extract was dried (Na_2SO_4–K_2CO_3) and the ether removed under reduced pressure. The oily residue was taken up in light petroleum (b. p. 40—60°; 3 ml.); when this solution was cooled in a solid carbon dioxide–methanol bath, 6-*phenylhexa*-3 : 5-*dien*-2-*ol* separated in needles (2 g.), which

after one recrystallisation had m. p. 65° (Found: C, 82·85; H, 8·25. $C_{13}H_{14}O$ requires C, 82·9; H, 8·1%). Light absorption in ethanol: Maxima at 2270, 2330, and 2800 A., ε 14,800, 9,200, and 32,300, respectively; inflection at 2850 A., ε 31,300. 6-Phenylhexa-3 : 5-dien-2-ol decomposes on storage, giving a yellow oil with an odour reminiscent of cinnamaldehyde.

1-*Phenylhexa*-1 : 3 : 5-*triene* (IX.)—1-Phenylhexa-2 : 4-dien-1-ol (4 g.) and finely ground potassium hydrogen sulphate (1 g.) were placed in a 50-ml. distilling flask with a wide side-arm and receiver. The apparatus was evacuated to 0·01 mm. and dipped into an oil-bath preheated to 100°. The temperature of the bath was then rapidly raised to 130°; 1-*phenylhexa*-1 : 3 : 5-*triene* distilled as a viscous oil (1·5 g.), b. p. 80°/0·01 mm., which solidified in the receiver and was immediately crystallised from light petroleum (b. p. 40—60°) giving fine needles, m. p. 56° (Found: C, 91·7; H, 7·9. $C_{12}H_{12}$ requires C, 92·3; H, 7·7%). Light absorption in ethanol: Maxima 2290, 2350, 2990, 3110, and 3250 A., ε 11,400, 10,700, 46,000, 55,000, and 43,000, respectively. If the distillate is kept before crystallisation, an increasing portion changes into a polymer, which is insoluble in light petroleum and can be precipitated from methanol by water as a white solid, m. p. >100°. When pure, 1-phenylhexa-1 : 3 : 5-triene remains unchanged for several days if stored under nitrogen.

Kinetic Measurements.—The kinetic measurements on the rearrangement of 1-phenylhexa-2 : 4-dien-1-ol to 6-phenylhexa-3 : 5-dien-2-ol were made by the spectrometric method previously described (cf. Braude, Jones, and Stern, *J.*, 1946, 396; Braude and Fawcett, *J.*, 1950, 800), a modified technique being used in which the runs are carried out directly in the absorption cell of a Beckman photoelectric spectrophotometer. The absorption cell is contained in a thermostatically controlled holder which fits into the cell compartment, and the light beam is allowed to fall on the cell only during the brief absorption measurements, by means of a shutter arrangement. Details of this technique will be described elsewhere. It is necessary to ensure that no detectable photochemical decomposition occurs during the total period of exposure to the ultra-violet light beam; this is done by exposing the solution after termination of a run to continuous illumination for an equivalent period and noting any further change in the light absorption. No detectable photochemical decomposition occurred with the phenylhexadienols, and the rate of isomerisation was not affected by the intermittent ultra-violet illumination. Some typical runs are reproduced below.

Rearrangement of 1-*phenylhexa*-2 : 4-*dien*-1-*ol in a* 0·001M-*solution of hydrochloric acid in aqueous dioxan. Carbinol concentration,* $0·2 \times 10^{-4}$ *g.-mol./l.*

(*a*) Dioxan concentration, 40% by volume; $t = 30°$.

Time, sec.	0	199	262	365	422	530	586	660	780	870	920	1100	10,000
$10^{-2}\varepsilon$ at 2510 A.	97	95	94	93	92	91	91	90	89	89	88	87	62
$10^{-2}\varepsilon$ at 2810 A.	22	70	83	103	114	131	138	148	162	173	183	192	263
10^4k, min.$^{-1}$ ...	—	663	672	670	683	680	672	665	668	678	673	667	—

Mean 10^4k (min.$^{-1}$): 673 ± 5.

(*b*) Dioxan concentration, 40% by volume; $t = 40°$.

Time, sec.	0	76	104	124	153	180	208	235	267	303	3000
$10^{-2}\varepsilon$ at 2810 A.	22·5	65	77·5	87·5	100	110	120	130	140	150	250
10^4k, min.$^{-1}$ ...	—	1630	1610	1630	1630	1620	1610	1630	1630	1620	—

Mean 10^4k (min.$^{-1}$): 1620 ± 10.

(*c*) Dioxan concentration, 60% by volume; $t = 40°$.

Time, min.	0	4	5·5	7	9	11	13	15·5	18·5	24	200
$10^{-2}\varepsilon$ at 2810 A.	21·5	63	78	90·5	106	120	134	149	163	184	254
10^4k, min.$^{-1}$ ...	—	480	497	495	496	495	502	510	502	497	—

Mean 10^4k (min.$^{-1}$): 495 ± 5.

We thank the Department of Scientific and Industrial Research for a grant (to J. A. C.).

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
SOUTH KENSINGTON, LONDON, S.W.7.

[*Received, February 9th*, 1951.]

464. *The Alkalimetric Determination of Metals with the Aid of Acid–Base Indicators. Part II.**

By J. F. Coetzee.

This paper deals with the determination of zinc, mercury, copper, and antimony by means of titration with standard alkali, as well as with the alkalimetric analysis of mixtures of mercury and copper with cadmium or cobalt. Completion of precipitation of the metal is determined with the aid of a suitable acid–base indicator. Similarly, free mineral acid is titrated in presence of zinc, mercury, and copper by application of an indicator of proper pH range. This principle has now been applied for the first time to the determination of antimony and to the quantitative analysis of mixtures of metals. The existing procedures for the determination of zinc, mercury, and copper have been substantially modified.

The underlying principles of the alkalimetric method have been treated in Part I (*loc. cit.*), which also dealt with the determination of aluminium, cadmium, and cobalt.

Determination of Zinc.—The fact that addition of alkali to zinc solutions at room temperature leads to precipitation of basic salts, has been well established (see, *e.g.*, Britton, *J.*, 1925, **127**, 2124). From the analytical point of view additional complication arises from the fact that this precipitate is soluble in excess of alkali. Ruoss (*Z. anal. Chem.*, 1896, **35**, 143) added excess of baryta, boiled, and back-titrated with hydrochloric acid. Simplification of the method by direct titration to the phenolphthalein end-point gave moderately accurate results with zinc bound to chlorine, but led to considerable under-titration in presence of sulphate (Kolthoff, "Massanalyse," Vol. II, 1928, p. 167). Kolthoff found that addition of barium chloride improved the titration, but even then the results were insufficiently accurate. He consequently proposed a back-titration method, which in turn suffered from the drawbacks that the zinc oxide precipitate retained adsorbed alkali very tenaciously, and that the phenolphthalein end-point was ill-defined (see below). Hence the accuracy of the method did not exceed 1%.

Determination of Mercury.—As with zinc, addition of alkali to mercuric solutions at room temperature results in basic salt formation (Britton, *loc. cit.*, p. 2150). Direct titration of mercuric chloride proved ineffective when colour indicators were used. The basic chlorides produced could not be quantitatively decomposed into oxide within the pH range attainable by direct titration. Further, the intense colour of these basic chlorides masked the end-point very seriously. Consequently, Rupp *et al.* (*Pharm. Zentr.*, 1926, **67**, 529) added excess of alkali and some hydrogen peroxide, and heated until the precipitate had been completely reduced to metallic mercury. After cooling, they back-titrated to the methyl-red or dimethyl-yellow end-points. Kolthoff (*op. cit.*) found that phenolphthalein could also be used, and considered the method to be accurate to 0·5%.

Determination of Copper.—(a) *Composition of precipitate.* The composition of the precipitate produced by adding alkali to cupric solutions has been a subject of much controversy (see Mellor, "A Comprehensive Treatise on Inorganic and Theoretical Chemistry," Vol. III, p. 261). Numerous basic salt structures have been reported, ranging in composition from $CuSO_4$,CuO,aq. to $CuSO_4$,14CuO,aq., with varying water contents; $Cu(OH)_2$ as such is only precipitated under carefully controlled conditions (Dawson, *J.*, 1909, **95**, 370). The composition of these precipitates has been investigated by electrometric, conductometric, and phase-rule studies, as well as by the colorimetric determination of pH; although the results are conflicting, certain facts have been definitely established. Electrometric studies (Britton, *loc. cit.*, pp. 2152, 2796) have indicated that the composition of the precipitate produced at room temperature is influenced by the manner in which the precipitant is added. A similar conclusion was reached by Pickering (*Chem. News*, 1883, **47**, 181; *J.*, 1883, **43**, 337; 1907, **91**, 1981) and by Carrière *et al.* (*Bull. Soc. chim.*, 1946, **13**, 396) from their colorimetric pH determinations. The author's results bear this out. Pickering also observed that the amount of base required to cause alkalinity to phenolphthalein at room temperature varied with the nature of the base employed; only baryta led to a permanent end-point, the neutralisation of other bases continuing for 2—3 days (cf. also Carrière *et al.*, *loc. cit.*).

Many phase-rule studies of the ternary system CuO–SO_3–H_2O have been carried out to determine which of the numerous basic salts reported actually existed. Conflicting results

* Part I, *J.*, 1951, 997.

were obtained (cf., *e.g.*, Bell and Taber, *J. Physical Chem.*, 1908, **12**, 171; Young and Stearn, *J. Amer. Chem. Soc.*, 1916, **38**, 1947; Britton, *loc. cit.*, p. 2796; Fowles, *J.*, 1926, 1845; Britton, *ibid.*, p. 2868; Bell and Murphy, *J. Amer. Chem. Soc.*, 1926, **48**, 1500). Nevertheless the existence of the basic sulphate $4CuO,SO_3,aq.$ has been established. Conductometric evidence (Chrétien and Heubel, *Compt. rend.*, 1944, **219**, 363) also indicates this structure. The author's results prove that under specified conditions this is the only stable basic salt of copper.

(b) *Determination of copper as oxide.* Ruoss (*loc. cit.*) titrated cupric solutions in the same manner as zinc solutions (above). The cupric oxide precipitate coagulated rapidly, and he back-titrated the mother-liquor with acid. Kolthoff (*op. cit.*) found the method accurate to *ca.* 1%. Carrière *et al.* (*Bull. Soc. chim.*, 1945, **12**, 75) titrated cupric sulphate directly to the phenolphthalein end-point, and claimed results concordant to 0·5% with those determined iodometrically. These authors apparently titrated at room temperature, and interpreted their results on the assumption that copper hydroxide was produced. Under these conditions the titre depends on the nature of the base employed and even on its mode of addition (see above), with the result that a reproducible end-point cannot be obtained. Further, the error introduced is much bigger than 0·5%.

Alkalimetric Analysis of Mixtures of Metals.—Two general methods are available for this purpose. First, a suitable reagent may often be employed to protect undesirable metals against attack by alkali, without affecting the metal to be determined. Secondly, it is evident from the relative magnitudes of hydroxide precipitation pH values that fractional precipitation of metal " hydroxides " may be effected by careful pH control. Only the second general method will be treated here. The mere separation of metals by pH control is relatively simple (see, *e.g.*, Gilchrist, *J. Res. Nat. Bur. Stand.*, 1943, **30**, 89), since the only requirement for this purpose is formation of insoluble precipitates. From the point of view of quantitative analysis, however, an additional requirement is that the precipitate should be of definite composition.

Experimental.

Free Mineral Acid Content of Metal-salt Solutions.—The electrometrically determined hydroxide precipitation pH values of the metals dealt with here were reported as follows for 0·02M-solutions (Britton, *Ann. Reports*, 1943, **40**, 45): Zn, 6·8—7·1; $Hg(NO_3)_2$, 2; $HgCl_2$, 7·3; Cu, 5·3; $CdSO_4$, 6·7; $CdCl_2$, 7·6; Co, 6·8.

Zinc. Free mineral acid can be determined in solutions diluted to <0·1M. with regard to zinc by titration with N-alkali to the dimethyl-yellow (pH 2·9—4·1), or preferably the bromophenol-blue (pH 3·0—4·6) end-point. If 0·1N-alkali is employed, the titration is best conducted to the methyl-red (pH 4·4—6·3) end-point in a solution diluted to <0·02M. with regard to zinc. As with the other amphoteric metal, aluminium, the titration should be conducted slowly, since any precipitate produced by rapid addition of reagent or inadequate agitation of solution redissolves with difficulty.

Mercuric. Use is made of the fact that the presence of halide ions causes a pronounced increase in the hydroxide precipitation pH value of this metal (cf. values above). Solutions <0·1M. with regard to mercury can be titrated with N-alkali in presence of an equivalent amount of chloride by using dimethyl-yellow as indicator. Solutions diluted to <0·02M. can be titrated with 0·1N-alkali to pH 3·8 with the aid of methyl-orange–xylene cyanol-F.F. screened indicator, provided that at least an equivalent amount of chloride be present. An excellent colour change may be obtained with the aid of bromocresol-green (pH 3·8—5·4), or preferably the mixed indicator for pH 5·1 (Kolthoff and Rosenblum, " Acid–Base Indicators," 1937, p. 173), provided that at least 3 times the equivalent amount of chloride be present.

Cupric. As in the case of cobalt, interference by the characteristic colour of the cupric ion may be sufficiently reduced by dilution. Determination of the free mineral acid content of cupric solutions brought to light an interesting phenomenon. Relatively low pH range indicators, such as dimethyl-yellow, methyl-orange, and bromophenol-blue, were extremely sluggish. Bromocresol-green gave an end-point of moderate definition, such as is to be expected from, say, methyl-orange when employed under usual conditions. Finally, a mixed indicator for the pH range 4·4—6·0 (B.D.H.) gave a well-defined end-point, although the hydroxide precipitation pH value of the solution employed (0·02M.) was 5·3. This indicated a definite lowering of the pH range of the " 4460 " indicator, a contention substantiated by electrometric measurements carried out with a Beckmann glass-electrode pH meter; *e.g.*, the orange intermediate colour of the " 4460 " indicator, which normally corresponds to pH 5·4, was obtained at the pH values 5·1, 4·9, and 4·7 in copper sulphate solutions of 0·001, 0·005, and 0·025M., respectively. A similar repression of the pH range of bromocresol-green was observed.

Bromocresol-green and the " 4460 " indicator are best employed in solutions diluted to <0·02M. with regard to copper.

Determination of Metals in Salt Solutions.—Zinc. As with aluminium, cadmium, and cobalt, zinc is best titrated in solutions of its nitrate. Standard solutions of zinc nitrate were prepared as follows: C.P. zinc (Coleman and Bell) was dissolved in 5N-nitric acid, and excess of acid removed by dropwise addition of sodium hydroxide solution until a permanent precipitate just appeared. A slight excess of acid, just sufficient to ensure a practicable titre, was then added, and the solution was boiled for several minutes, cooled, and made up to the required volume.

Results accurate to *ca.* 0·1% have been obtained by the following procedure: (*a*) The approximate titre is determined by titrating hot to the phenolphthalein end-point. The relatively poor definition of this end-point is probably due to zincate formation, since it corresponds to slight over-titration; further, the full alkaline colour of the indicator cannot be developed. (*b*) Another aliquot portion of the solution is then titrated hot to 0·3—0·4 ml. before the approximately determined end-point, cooled, and the titration completed to the end-point of the mixed indicator for pH 9·0 (Kolthoff and Rosenblum, *op. cit.*). This indicator gives a well-defined end-point which corresponds very closely to the theoretical titre for zinc oxide. The method is applicable over a wide concentration range. The results obtained with this method are summarised below.

Zn, g.-ions per l.	Vol. titrd., ml.	Alkali, N.	Acid, ml.	Acid + Zn, ml.	Zn, ml. Found.	Zn, ml. Calc.	Error, ml.
0·6135	20	0·9782	3·26	28·32	25·06	25·09	−0·03
0·6096	20	0·9782	3·43	28·35	24·92	24·93	−0·01
0·07233	20	0·1196	5·21	29·40	24·19	24·18	+0·01
0·07185	20	0·1196	4·80	28·83	24·03	24·03	0
0·01580	100	0·1196	3·45	29·84	26·39	26·42	−0·03
0·01548	100	0·1196	2·87	28·71	25·84	25·87	−0·03

The presence of chloride results in slight under-titration, though the error is very much less than for cadmium and cobalt. It may be practically eliminated by conducting the major part of the titration boiling hot and approaching the end-point as closely as possible before cooling.

Sulphate should be removed by addition of barium nitrate solution in excess. It is important to add the barium at room temperature, for if it is added to the hot solution, considerable under-titration results. Alternatively, the sulphate solution may be added to the barium, with thorough agitation of the latter. The resulting zinc nitrate is then titrated in the presence of the precipitate.

Free mineral acid alone, and acid and zinc together, may be conveniently titrated in the same aliquot solution. The yellow alkaline colour of methyl-red does not appreciably affect the colour change of the " 9·0 " indicator from yellow to violet, provided a relatively small amount of methyl-red is employed.

Mercuric. Standard solutions of mercuric nitrate were prepared by dissolving C.P. mercury (Merck's *pro analysi*) in excess of 4N-nitric acid, boiling until oxidation of mercurous salt was complete, and then proceeding as with zinc.

Mercuric can be determined as oxide with an accuracy of *ca.* 0·1% by direct titration of its nitrate solution, any indicator being used of pH range between those of bromocresol-green (3·8—5·4) and thymol-blue (8·0—9·6). The orange precipitate settles rapidly, leaving the supernatant liquor almost clear. Nevertheless, it is advantageous to use an indicator with a violet or blue alkaline colour, which is better visible in presence of the orange precipitate than a red, yellow, or green one: thymol-blue, bromothymol-blue (pH 6·0—7·6), and bromocresol-purple (pH 5·2—6·8) are suitable.

Titration at room temperature leads to slight under-titration when a high-range indicator is used, such as thymol-blue; this error becomes more serious with increasing dilution. With very dilute solutions the titre is furthermore influenced by the mode of addition of alkali. The use of low-range indicators leads to considerable under-titration with relatively concentrated solutions, but the under-titration error diminishes with increasing dilution. Hence the titration is best conducted at a high temperature, which eliminates the under-titration error and also promotes coagulation of the precipitate. If the concentration of the solution can be adjusted at will and the pH range of the indicator used is immaterial, it is best to titrate hot at a concentration *ca.* 0·05M. to the bromothymol-blue end-point.

A very simple modification of the above method permits of the titration of mercuric chloride solutions. Chloride is precipitated by addition of excess of silver nitrate, and mercuric salt determined in presence of the resulting precipitate by titrating to the bromocresol-purple end-point, which is unaffected by the silver in excess; silver oxide is not precipitated until pH 7·5—8 is reached. In this connection the following observations are of importance: (*a*) if chloride is precipitated before addition of alkali, the results are low and not accurately reproducible. This may be attributed to occlusion of mercury by the silver chloride precipitate and/or the appreciable solubility of silver chloride in mercuric nitrate solutions (see Mellor, *op. cit.*, p. 398); (*b*) if the major part of the titration is conducted hot and the silver added just before the end-point, the basic mercuric chloride often fails to separate; this leads to considerable under-titration, especially with relatively dilute solutions.

Hence the following procedure is recommended: (i) the approximate titration value is determined by precipitating chloride before adding alkali, and then titrating hot to the bromocresol-purple end-point; (ii) the major part of the titration is conducted at room temperature in presence of chloride, and excess of silver is added just before the approximately determined end-point is reached: $x\mathrm{HgO},y\mathrm{HgCl_2} + 2y\mathrm{AgNO_3} \longrightarrow x\mathrm{HgO} + 2y\mathrm{AgCl} + y\mathrm{Hg(NO_3)_2}$. The silver chloride precipitate coagulates rapidly, and does not darken upon exposure to light (see, *e.g.*, Mellor, *op. cit.*, p. 409). The solution is then heated just to boiling, and the titration continued to the bromocresol-purple end-point, which is vivid and reproducible to 0·1%.

The final addition of alkali after chloride has been precipitated may also be carried out at room temperature without impairing the accuracy of the results. However, under these conditions the indicator is very rapidly adsorbed by the silver chloride precipitate, and an unduly large amount must be employed. The tendency of silver chloride to adsorb the indicator is greatly reduced by heating.

The results obtained by titrating mercuric nitrate and chloride solutions are tabulated below. Al titrations were performed in 100-ml. portions.

Hg, g.-ions per l.	Alkali, N.	Acid, ml.	Acid + Hg, ml.	Hg, ml. Found.	Hg, ml. Calc.	Error, ml.
0·1183	0·9780	4·36	28·52	24·16	24·19	−0·03
0·1167	0·9780	4·34	28·17	23·83	23·86	−0·03
0·1365	0·1196	3·62	26·44	22·82	22·82	0
0·01348	0·1196	2·80	25·33	22·53	22·54	−0·01
0·01573 *	0·1196	0	26·38	26·38	26·38	0
0·01464 *	0·1196	0	24·45	24·45	24·47	−0·02

* Mercuric chloride (Merck's *pro analysi*) solutions.

Cupric. If copper sulphate is titrated at ordinary rate with alkali at temperatures below *ca.* 50°, no indicator gives an end-point suitable for analytical purposes. At higher temperatures, however, any indicator between chlorophenol-red (pH 4·6—7·0) and thymolphthalein (pH 9·3—10·5) gives a well-defined, stable end-point, corresponding to the consumption of exactly 1·5 equivs. of alkali. Hence under these conditions the basic sulphate $CuSO_4,3CuO,aq.$ is precipitated. The precipitate coagulates rapidly, leaving the supernatant liquor almost clear. Nevertheless, it is advisable to use an indicator with a violet or red alkaline colour, which is better visible in the presence of the greenish-blue precipitate than a yellow, green, or blue one.

The titre is independent of concentration over a wide range. If the concentration can be adjusted at will, and the pH range of the indicator used is immaterial, it is recommended to titrate the solution between the concentration limits 0·1—0·01M. at a temperature above 60°, phenolphthalein or preferably *o*-cresol-red (pH 7·0—8·8) being used as indicator.

Titration of cupric chloride and nitrate at room temperature gives rise to the same phenomena as with the sulphate. At higher temperatures, however, basic nitrate precipitates gradually darken with formation of cupric oxide. Basic chloride precipitates are more stable, though the titre is not quite independent of the concentration. This is in harmony with the general observation that the order of stability of basic salts usually follows the sequence sulphate > chloride > nitrate.

The low solubility and remarkable stability of the basic sulphate $CuSO_4,3CuO,aq.$ lead to its preferential precipitation from solutions of the nitrate and chloride, provided sufficient sulphate is also present. Results accurate to <0·1% have been obtained with solutions prepared by dissolving C.P. electrolytic copper (Kagerah) in nitric acid and adding the required amount of sodium or potassium sulphate. Even high concentrations of nitrate and chloride do not affect the titration at all.

The results obtained by this method are summarised below. All titrations were conducted in 100-ml. portions.

Cu, g.-ions per l.	Alkali, N.	Acid, ml.	Acid + Cu, ml.	Cu, ml. Found.	Cu, ml. Calc.	Error, ml.
0·1664	0·9782	6·31	31·83	25·52	25·52	0
0·1652	0·9782	5·20	30·51	25·31	25·33	−0·02
0·01920	0·1196	5·15	29·20	24·05	24·07	−0·02
0·01893	0·1196	5·64	29·38	23·74	23·74	0
0·001680	0·01047	2·38	26·41	24·03	24·07	−0·04
0·001667	0·01047	3·00	26·86	23·86	23·89	−0·03

This method has been compared with the iodometric one and proved to possess certain definite advantages, such as the brilliance of the end-point, the reliability and stability of standard solutions of alkali as compared with thiosulphate solutions, and the inexpensive reagents required.

The reaction between Cu^{++}, SO_4'', and OH' on the one hand, and between Cu^{++} and I' on the other, provides a useful link between alkalimetric and iodometric standards.

Antimony in tartar emetic. As hydrated tartar emetic is efflorescent, standard solutions are best prepared from the anhydrous compound. It is not very soluble in water, and preparation of a 0·2M-solution is just possible at room temperature. Good results can be obtained by titrating the solution boiling hot to the thymolphthalein (pH 9·3—10·5) end-point, which corresponds to the consumption of 1 equiv. of alkali: $2C_4H_4O_4K(SbO) + 2MOH \longrightarrow Sb_2O_3 + C_4H_4O_4K_2 + C_4H_4O_4M_2 + H_2O$. The results obtained by titrating anhydrous tartar emetic (AnalaR) are summarised below. All titrations were performed with 0·1196N-alkali.

Sb, g.-ions per l.	Vol. titrd., ml.	Sb, ml. Found.	Sb, ml. Calc.	Error, ml.	Sb, g.-ions per l.	Vol. titrd., ml.	Sb, ml. Found.	Sb, ml. Calc.	Error, ml.
0·2000	10	16·76	16·72	+0·04	0·0800	20	13·39	13·38	+0·01
0·1500	10	12·55	12·54	+0·01	0·0400	50	16·70	16·72	−0·02
0·1000	20	16·73	16·72	+0·01	0·0200	100	16·69	16·72	−0·03

The same procedure applied at room temperature leads to over-titration.

The alkalimetric determination of antimony in tartar emetic provides a useful link between alkalimetric and iodometric standards (cf. copper).

Alkalimetric Analysis of Mixtures of Metals.—Free mineral acid–mercuric–cupric–cobalt mixtures. (i) Free mineral acid is titrated in presence of at least 3 times as much chloride as the mercuric content of

the solution, bromocresol-green (pH 3·8—5·4) or preferably the B.D.H. "4460" indicator being used. For optimum results the solution must be diluted to <0·02M. with regard to copper.

(ii) Free mineral acid + mercuric is titrated in absence of chloride at room temperature to the bromocresol-green end-point. For optimum results the solution must be diluted to <0·02M. with regard to copper. However, excessive dilution, especially of solutions of low mercury content, leads to under-titration. If chloride is present, it must be removed by addition of silver (see p. 2100).

(iii) Free mineral acid + mercuric + cupric is titrated slowly to the stage represented by the above, but without addition of indicator; sodium or potassium sulphate is then added in amount equivalent to at least 5 times the copper content of the solution, and the boiling solution titrated slowly to the chlorophenol-red (pH 4·6—7·0) end-point. For optimum results the solution must be diluted to <0·01M. with regard to cobalt.

(iv) For free mineral acid + mercuric + cupric + cobalt the solution is titrated to the stage represented by the above, but without addition of indicator. The mixed precipitate of mercuric oxide and basic cupric sulphate is filtered off and washed with hot water. Sulphate is precipitated in the cold filtrate by adding excess of chloride-free barium nitrate solution (cf. zinc), and cobalt determined in presence of this precipitate by alkalimetric titration (Part I, *loc. cit.*).

Free mineral acid–mercuric–cupric–cadmium mixtures. The procedure is identical with the one outlined above. The final titration of cadmium should be conducted in absence of sulphate. Titration to the basic sulphate stage (Carrière, Guiter, and Portal, *Bull. Soc. chim.*, 1946, **13**, 99) is much less accurate, since basic cadmium sulphate is unstable to variation in concentration, temperature, and pH. The definition of the end-point deteriorates rapidly with increasing dilution and rise in temperature, and the titre is determined by the mode of addition of alkali. Results are invariably too high owing to partial decomposition of basic sulphate into hydroxide.

UNIVERSITY OF THE ORANGE FREE STATE,
BLOEMFONTEIN, SOUTH AFRICA.

[*Received, February 26th*, 1951.]

---

465. *The Ionisation of Triarylcarbinols in Strong Acids and the Definition of a New Acidity Function.*

By V. GOLD and B. W. V. HAWES.

Expressions have been derived and experimentally tested for the dependence of the degree of ionisation of a triarylcarbinol according to

$$R{\cdot}OH + 2H_2SO_4 \rightleftharpoons R^+ + H_3O^+ + 2HSO_4^-$$

or

$$R{\cdot}OH + H_2SO_4 \rightleftharpoons R^+ + H_2O + HSO_4^-$$

upon the composition of the medium, in the case of strong aqueous acids and acid solvent mixtures of low water content. An acidity function (J_0) has been defined (and tabulated for H_2SO_4–H_2O mixtures) which plays for the triphenylcarbinol type of ionisation a rôle analogous to that of Hammett's H_0 function for the ionisation of electrically neutral Brønsted bases. Some applications of this acidity function to compounds other than triarylcarbinols are briefly considered.

MANY organic substances behave as simple monoacid bases when dissolved in strong acids (Hammett, "Physical Organic Chemistry," New York, 1940, Chap. IX). In concentrated sulphuric acid as solvent they give rise to two particles, as can be shown by cryoscopy (see Gillespie, Hughes, and Ingold, *J.*, 1950, 2473, where a literature summary is also given). The dependence of the degree of ionisation on the composition of the medium may be satisfactorily expressed in terms of Hammett's acidity function (Hammett and Deyrup, *J. Amer. Chem. Soc.*, 1932, **54**, 2721).

Triphenylcarbinol typifies a different kind of reversible ionisation in strong acid. The freezing-point depression in sulphuric acid is in this case four times that produced by an ideal inert solute (Hantzsch, *Z. physikal. Chem.*, 1907, **61**, 257; Hammett and Deyrup, *J. Amer. Chem. Soc.*, 1933, **55**, 1900) and the light absorption of the solution is identical with that of triphenylmethyl chloride in sulphur dioxide and other non-aqueous ionising solvents (Hantzsch, *Ber.*, 1921, **54**, 2573). The ionisation has plausibly been represented in the form

$$Ph_3C{\cdot}OH + 2H_2SO_4 \rightleftharpoons Ph_3C^+ + H_3O^+ + 2HSO_4^-$$

Baeyer suggested as early as 1905 (*Ber.*, **38**, 569) that in this case a triphenylcarbonium hydrogen sulphate, with an abnormal "carbonium valency" between the two groups, is formed. The

dependence of the degree of ionisation on the composition of the medium would be expected to be different from that for the monoacid bases, and this has been shown to be so for certain substituted derivatives of triphenylcarbinol by Westheimer and Kharasch (*J. Amer. Chem. Soc.*, 1946, **68**, 1871) and by Murray and Williams (*J.*, 1950, 3322).

The present study was undertaken to examine the nature of this dependence more precisely. The experimental data considered in this connection are (i) published colorimetric indicator measurements on trinitrotriphenylcarbinol in sulphuric acid–water mixtures, carried out by Murray and Williams (*loc. cit.*) in a simultaneous investigation, and (ii) new spectrophotometric measurements of the degree of ionisation of triphenylcarbinol and of a simple monoacid base (4-chloro-2-nitroaniline) over certain ranges of composition in the ternary solvent system sulphuric acid–acetic acid–water.

The interest in this type of ionisation is not exhausted by the consideration of the typical example triphenylcarbinol. We may recall that an ionisation

$$XOH + 2H_2SO_4 \rightleftharpoons X^+ + H_3O^+ + 2HSO_4^-$$

is required to produce species such as NO_2^+, Br^+, Cl^+, HSO_3^+, $(acyl)^+$, OH^+—all of which have recently received attention as probable reaction intermediates—from nitric acid (reviewed by Gillespie and Millen, *Quart. Reviews*, 1948, **2**, 277), hypobromous acid (Derbyshire and Waters, *J.*, 1950, 564), hypochlorous acid (de la Mare, Hughes, and Vernon, *Research*, 1950, **3**, 192, 242; Derbyshire and Waters, *J.*, 1951, 73), sulphuric acid (Stubbs, Williams, and Hinshelwood, *J.*, 1948, 1065; Brand, *J.*, 1950, 1004), carboxylic acids (Treffers and Hammett, *J. Amer. Chem. Soc.*, 1937, **59**, 1708; Newman *et al.*, *ibid.*, 1941, **63**, 2431; 1942, **64**, 2324; 1945, **67**, 704; Kuhn and Corwin, *ibid.*, 1948, **70**, 3370; Kuhn, *ibid.*, 1949, **71**, 1575), and hydrogen peroxide (Derbyshire and Waters, *Nature*, 1950, **165**, 401), respectively.

It is noteworthy that the type of ionisation considered for triphenylcarbinol is not basic behaviour in the sense of the Brønsted–Lowry definition. One may fit these examples into the Brønsted–Lowry scheme by assuming that the course of the ionisation is proton transfer to the carbinol and subsequent dehydration of the conjugate acid, or by assuming other, less plausible, mechanisms. We have found no evidence for the existence of the undehydrated conjugate acid $[Ph_3C{\cdot}OH_2]^+$, although there may be cases where the analogous compound may exist (cf. the results of Treffers and Hammett, *loc. cit.*, for 2 : 6-dimethylbenzoic acid and 3 : 5-dibromo-2 : 4 : 6-trimethylbenzoic acid; $Br\overset{+}{O}H_2$, Derbyshire and Waters, *J.*, 1950, 564; $NO_2{\cdot}\overset{+}{O}H_2$, Halberstadt, Hughes, and Ingold, *J.*, 1950, 2441). It is, however, unsatisfactory that the behaviour of triphenylcarbinol, as expressed in a thermodynamic equation, may only be described as basic if a hypothetical reaction mechanism is assumed for it. In the absence of a clearer term * we would propose the name "secondary base" for triphenylcarbinol and other compounds ionising in this way, the conjugate acid being the water molecule formed. It is interesting that this extended definition is necessary to reconcile basicity in hydroxyl-containing bases (the *real* bases according to older views) with the Brønsted–Lowry definition, whereas the concept of secondary acids is necessary to fit the hydrogen acids into Lewis's scheme of acids and bases (cf. Bell, *Quart. Reviews*, 1947, **1**, 113).

Experimental.

Materials.—Acetic acid was purified and dried by Orton and Bradfield's method (*J.*, 1927, 983). The purity was checked by freezing-point determinations and only samples having f. p. > 16·40° (*i.e.*, containing less than 0·1% of water) were used. The purified acid was transparent to wave-lengths greater than 2400 A., although no exact measurements were attempted with it below λ 2500 A.

Sulphuric acid (100%) was prepared by dilution of sulphur dioxide-free oleum with 98% AnalaR sulphuric acid to the cessation of fuming at a low temperature (Brand, *J.*, 1946, 585). The composition was checked by freezing-point determinations, only acids of f. p. within 0·08° of the maximum corresponding to the composition H_2SO_4 being used. The oleum for this preparation was obtained by addition of potassium persulphate to a dilute commercial oleum and distillation of sulphur trioxide from it into 98% AnalaR sulphuric acid in an all-Pyrex apparatus (cf. Brand, *J.*, 1950, 997). Sulphuric acid prepared in this way was transparent to light above λ 2300 A. and did not show appreciable absorption due to sulphur dioxide (cf. Gold and Tye, *J.*, 1950, 2932).

Solvent mixtures were made up by weight, and compositions are stated as weight percentages of the solution. Attention was paid to avoiding the complications of the ageing effect of mixtures of acetic acid and sulphuric acid reported by Tolbert and Branch (*J. Amer. Chem. Soc.*, 1947, **69**, 1083).

Triphenylcarbinol and 4-chloro-2-nitroaniline were purified by repeated crystallisations from benzene

* The term pseudo-base advocated by Hammett (*Chem. Reviews*, 1937, **13**, 63) is also in use with a different meaning and is therefore undesirable.

and water, respectively, and the progress of the purification checked by absorption-spectrum measurements (Figs. 1, 2, and 5).

Measurements.—Extinction coefficients in the near ultra-violet and visible spectral regions were measured by means of a Hilger "Uvispek" Photoelectric Spectrophotometer, fused quartz cells of the design shown in Fig. 3 being used. The matching of the cells was checked by comparison of the internal lengths and of their transmission over the whole spectral region investigated. Minor mechanical alterations were made to the instrument in order to adapt it for use with these cells. No accurate temperature control was maintained during the measurements, the results given referring for the most

FIG. 1.

Absorption spectra of 4-chloro-2-nitroaniline: (A) in acetic acid, (B) in sulphuric acid (100%).

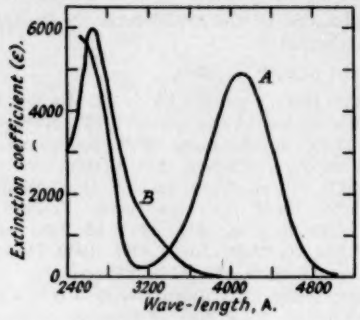


FIG. 2.

Absorption spectrum of triphenylcarbinol in acetic acid.

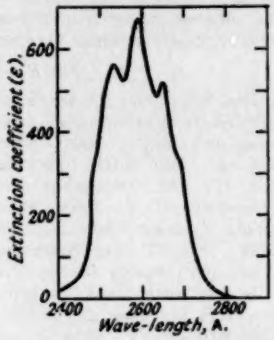


FIG. 3.

Spectrophotometer absorption cell.

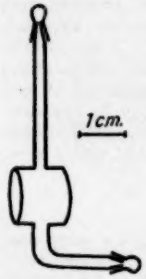
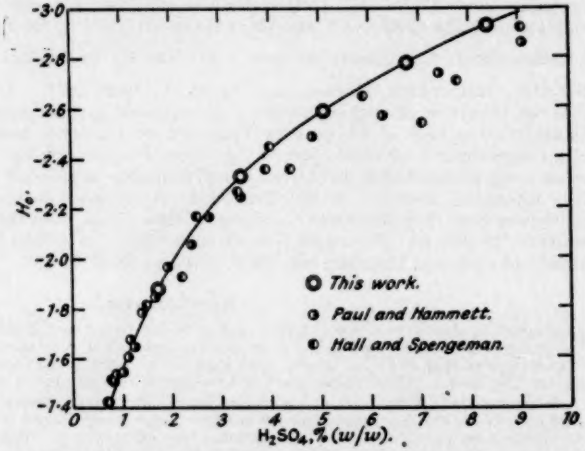


FIG. 4.

The acidity function (H_0) of solutions of sulphuric acid in acetic acid.



part to a temperature of 20° ±3°. Extinction coefficients (ε) are defined by the usual relation $\log_{10} I_0/I = \varepsilon cl$ (l = thickness of absorbing layer in cm., c = stoicheiometric concentration of solute, in moles/l.). None of the spectra of the solutions examined changed measurably with time.

Colorimetric measurements were carried out with a Hilger Visible "Spekker" Absorptiometer in conjunction with filters to limit the transmitted wave-band of light from a filament lamp. Such measurements were used only in cases where it was desired to check the absence of a change in the absorption spectrum over certain regions of solvent composition or to confirm the stability of certain solutions on storage.

Evaluation of Ionisation Ratios.—Ionisation ratios used in the calculation of acidity functions and of ionisation constants were obtained from the spectrophotometric measurements, the relationship $[\text{Ion}]/[\text{Base}] = (\varepsilon - \varepsilon_{\text{Base}})/(\varepsilon_{\text{Ion}} - \varepsilon)$ being used. The reference spectra of the ion and base were

obtained from solutions in 98% or 100% sulphuric acid and acetic acid respectively (cf. Flexser, Hammett, and Dingwall, *J. Amer. Chem. Soc.*, 1935, **57**, 2103). The concentration of 4-chloro-2-nitroaniline was usually in the range 10^{-4}—10^{-5}M., that of triphenylcarbinol $\sim 10^{-5}$M. It has been reported by these workers that solvent changes not only alter the ionisation ratio but also affect the wave-length of the absorption bands, and various procedures have been adopted to minimise the effect of this complication (see also Brand, *J.*, 1950, 997). Our own procedure, which was simplified by the choice of indicators the two forms of which absorbed strongly in different spectral regions only, is based on the following considerations:

Let ε_λ stand for the extinction coefficient of the indicator in the solution examined, and $\varepsilon_\lambda^\circ$ for that of the absorbing form of the indicator at a wave-length λ. If there is no solvent effect on the position of the spectrum, the fraction (a) of indicator in the absorbing form will be given by $a = \varepsilon_\lambda/\varepsilon_\lambda^\circ$, but if the spectrum in the solvent examined is displaced by an amount $\Delta\lambda$ relative to the reference spectrum of the absorbing form, then

$$a = \varepsilon_{(\lambda+\Delta\lambda)}/\varepsilon_\lambda^\circ$$

where

$$\varepsilon_{(\lambda+\Delta\lambda)} = \varepsilon_\lambda + \int_\lambda^{\lambda+\Delta\lambda} \frac{\partial\varepsilon}{\partial\lambda}\,d\lambda \quad = \varepsilon_\lambda + \int_\lambda^{\lambda+\Delta\lambda} \sigma_\lambda \,.\, d\lambda$$

Assume that the slope (σ_λ) of the curve of extinction coefficient against wave-length is constant over the short range λ to $\lambda + \Delta\lambda$, then

$$\varepsilon_{(\lambda+\Delta\lambda)} = \varepsilon_\lambda + a\int_\lambda^{\lambda+\Delta\lambda} \sigma_\lambda^\circ \,.\, d\lambda \quad = \varepsilon_\lambda + a\sigma_\lambda^\circ \,.\, \Delta\lambda$$

where σ_λ° is the corresponding slope of the curve for the pure absorbing form of the indicator. Therefore

$$\varepsilon_\lambda/\varepsilon_\lambda^\circ = a(1 - \sigma_\lambda^\circ \,.\, \Delta\lambda/\varepsilon_\lambda^\circ)$$

If it is possible to choose two wave-lengths, λ_1 and λ_2, at which the slopes $\sigma_{\lambda_1}^\circ$ and $\sigma_{\lambda_2}^\circ$ do not change rapidly with wave-length, such that

$$\sigma_{\lambda_1}^\circ/\varepsilon_{\lambda_1}^\circ = -\sigma_{\lambda_2}^\circ/\varepsilon_{\lambda_2}^\circ$$

then

$$a = (\varepsilon_{\lambda_1}/\varepsilon_{\lambda_1}^\circ + \varepsilon_{\lambda_2}/\varepsilon_{\lambda_2}^\circ)/2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

and if $a \ll 1$ and $\varepsilon_{\text{"non-absorbing"}} \ll \varepsilon_{\text{absorbing}}$

$$\frac{[\text{absorbing form}]}{[\text{"non-absorbing" form}]} = \frac{a}{1-a} \sim \left\{\left(\frac{\varepsilon - \varepsilon_{\text{"non-abs."}}}{\varepsilon_{\text{abs.}} - \varepsilon}\right)_{\lambda_1} + \left(\frac{\varepsilon - \varepsilon_{\text{"non-abs."}}}{\varepsilon_{\text{abs.}} - \varepsilon}\right)_{\lambda_2}\right\}\Big/2 \quad . \quad . \quad (2)$$

Either equation (1) or (2) could be applied to our indicator measurements, with $\lambda_1 = 4000$ A. and $\lambda_2 = 4200$ A. in the case of 4-chloro-2-nitroaniline, and with $\lambda_1 = 4100$ A. and $\lambda_2 = 4200$ A. for triphenylcarbinol.

We may stress that the particular points chosen should only be subject to small solvent effects (ε° = large; $|\sigma^\circ|$ = small), yet the two members of each pair should be affected in *opposite* senses if, as has been reported, the solvent effect consists in a lateral displacement of the absorption curve. Nevertheless, the values of log [Ion]/[Base] calculated from the individual points of such pairs differed at the most by 0·03 unit only. Our values for the logarithm of the *mean* are therefore unlikely to be seriously in error from this source of complication.

TABLE I.

Some acidity functions of the system acetic acid–sulphuric acid–water, 4-chloro-2-nitroaniline being used as indicator.

[Added water], M.	H_2SO_4, %	ε_{4000}	ε_{4200}	$\log([BH^+]/[B])_{mean}$	$-H_0$
0	0	4700	4700	—	—
,,	1·73	460·5	456·0	0·97	1·88
,,	3·43	177·9	179·0	1·42	2·33
,,	5·11	100·0	99·8	1·68	2·59
,,	6·76	68·0	65·5	1·87	2·78
,,	8·39	50·0	45·9	2·02	2·93
,,	100	6·06	1·27	—	—
0·111	1·73	485	491	0·94	1·85
,,	3·43	193·0	194·9	1·37	2·28
,,	5·11	108·1	108·9	1·64	2·55
,,	6·76	71·4	69·3	1·84	2·75
,,	8·39	51·5	47·9	2·00	2·91
0·222	1·73	574	586	0·85	1·76
,,	3·43	224	227	1·30$_5$	2·21$_5$
,,	5·11	121·1	121·9	1·59	2·50
,,	6·76	78·0	76·1	1·80	2·71
,,	8·39	55·5	52·3	1·97	2·88
0·555	1·73	975	1009	0·57	1·48
,,	3·43	370	381	1·07	1·98
,,	5·11	139·0	139·9	1·52$_5$	2·43$_5$
,,	6·76	113·0	113·2	1·62	2·53
,,	8·39	76·0	74·1	1·81	2·72

TABLE II.

The ionisation of triphenylcarbinol in some acetic acid–sulphuric acid–water mixtures.

$[H_2O]_{added}$	$[H_2O]_{Total}$*	H_2SO_4, %	H_0	$2H_0 + \log [H_2O]_{Total}$*	ε_{4100}	ε_{4300}	$\log ([R^+]/[ROH])_{max.}$
0	0·032	0	—	—	0·0	0·0	—
,,	,,	0·78	−1·46	−4·42	1,158	1,121	−1·49
,,	,,	1·00	−1·58	−4·66	2,130	2,060	−1·21
,,	,,	1·49	−1·79	−5·08	5,350	5,200	−0·76
,,	,,	2·26	−2·05	−5·60	11,940	11,550	−0·32
,,	,,	3·00	−2·25	−6·00	17,010	16,650	−0·06
,,	,,	3·16	−2·28	−6·06	18,100	17,550	−0·01
,,	,,	4·16	−2·45	−6·40	28,020	27,350	+0·52
,,	—	100	—	—	36,180	35,840	—
0·111	0·143	1·73	−1·85	−4·54	1,214	1,191	−1·46
,,	,,	3·43	−2·28	−5·40	8,652	8,426	−0·51
,,	,,	5·11	−2·55	−5·94	20,770	20,340	+0·12
,,	,,	6·76	−2·75	−6·34	27,050	26,310	+0·46
,,	,,	8·39	−2·91	−6·66	29,910	29,110	+0·66
0·222	0·254	1·73	−1·76	−4·12	571	550	−1·80
,,	,,	3·43	−2·215	−5·03	4,223	4,109	−0·88
,,	,,	5·11	−2·50	−5·60	13,770	13,430	−0·22
,,	,,	6·76	−2·71	−6·02	23,960	23,150	+0·28
,,	,,	8·39	−2·86	−6·32	29,340	28,880	+0·63
0·555	0·587	1·73	−1·48	−3·19	125	118	−2·47
,,	,,	3·43	−1·98	−4·19	1,021	991	−1·54
,,	,,	5·11	−2·435	−5·10	4,362	4,247	−0·87
,,	,,	6·76	−2·53	−5·29	10,140	9,868	−0·41
,,	,,	8·39	−2·72	−5·67	16,610	16,180	−0·08

* The significance of these columns is given in the Discussion (p. 2110).

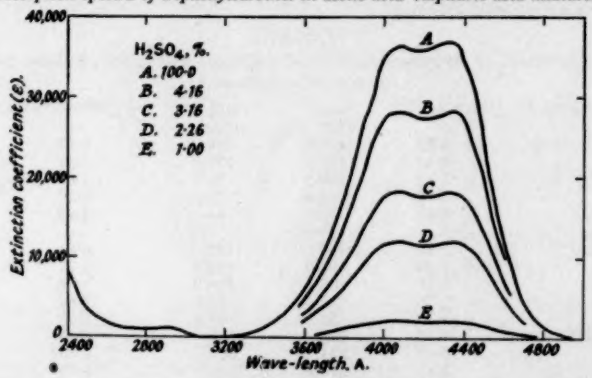
The acidity function H_0 was calculated from the ionisation ratios for 4-chloro-2-nitroaniline by means of Hammett's defining equation

$$H_0 = pK_a + \log [B]/[BH^+]$$

where pK_a, the negative logarithm of the acidity constant of the acid $[NO_2{\cdot}C_6H_3Cl{\cdot}NH_3]^+$, was taken to have the value −0·91 (Paul and Hammett, *J. Amer. Chem. Soc.*, 1936, **58**, 2182). The exact value of this does not affect the argument concerning the mechanism of ionisation of triphenylcarbinol. The results for the H_0 measurements are summarised in Table I, and those for the ionisation of triphenylcarbinol in Table II. In Fig. 4 our values for the H_0 function of some mixtures of acetic and sulphuric acids are plotted against the solvent composition, together with the results of earlier investigations based on colorimetric measurements (Paul and Hammett, *loc. cit.*; Hall and Spengeman, *J. Amer. Chem. Soc.*, 1940, **62**, 2487).

FIG. 5.

Absorption spectra of triphenylcarbinol in acetic acid–sulphuric acid mixtures.



DISCUSSION.

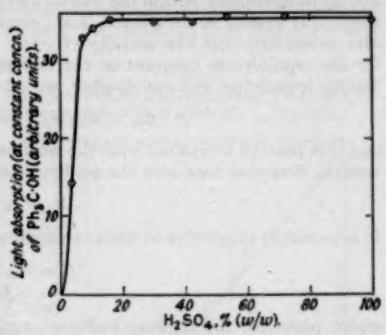
I. *The Identity of the Ion Formed.*—The absorption spectrum of triphenylcarbinol in acetic acid consists of a triple-peaked band centred around λ 2590 A. ($\varepsilon_{max.}$ = 660) with no detectable absorption above λ 3300 A. It is almost identical with the recorded spectrum of triphenylcarbinol in ethanol (Orndorff, Gibbs, McNulty, and Shapiro, *J. Amer. Chem. Soc.*, 1927, **49**,

1541) and may be attributed to the carbinol molecule. On addition of sulphuric acid to the solvent the absorption is intensified over the whole of the observed ultra-violet and visible region. In particular, a new double-peaked absorption band appears near λ 4200 A. (maxima at λ 4080 and 4310 A.; extinction coefficients 36,400 and 37,360, respectively). The position of this band remains remarkably little altered on changing the composition of the medium (Fig. 5). The absorption intensity remains constant in media containing more than ~16% w/w of sulphuric acid (Fig. 6).

If the light absorption of triphenylcarbinol in sulphuric acid–water mixtures is examined it is found that increasing water content of the medium leaves the absorption intensity unaffected until, in media containing more than ~40% of water, the acidity gets so low that the conversion of the molecule into the triphenylcarbonium ion is no longer complete and, since the un-ionised molecule is insoluble in aqueous sulphuric acid, triphenylcarbinol separates out.

FIG. 6.

Light absorption of solutions of triphenylcarbinol in acetic acid–sulphuric acid mixtures.



These two sets of observations suggest that only two forms of triphenylcarbinol are present in the various solutions in a sufficiently high concentration for their light absorption to matter, *viz.*, the triphenylcarbinol molecule (in the solvents of low acidity) and the coloured species into which the substance is completely converted in the highly acidic solvents. From the cryoscopic measurements it is extremely probable that this species is the triphenylcarbonium ion, and this conclusion is strengthened by the identical absorption spectra obtained with triphenylmethyl halides under ionising conditions. The simple medium dependence of the spectrum makes it very unlikely that the ion $Ph{\cdot}CO_2H_2^+$, a third species, is also present in the acid solutions of weaker dehydrating power to any appreciable extent, even though the light absorption of this ion would be expected to be similar to that of the triphenylcarbonium ion. The ionisation of triphenylcarbinol, also in solutions of lower acidity than that for which the quantitative formation of triphenylcarbonium ion has been established cryoscopically, will therefore be represented by the equations

$$Ph_3C{\cdot}OH + H_2SO_4 \rightleftharpoons Ph_3C^+ + H_2O + HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad (I)$$

or

$$Ph_3C{\cdot}OH + 2H_2SO_4 \rightleftharpoons Ph_3C^+ + H_3O^+ + 2HSO_4^- \quad . \quad . \quad . \quad . \quad . \quad (II)$$

According to the medium employed the first or the second equation will be found more convenient.

II. *The Ionisation of Triarylcarbinols in Aqueous Media and the Definition of the Acidity Function* J.—It is in this case more convenient to consider the equilibrium (I) in order to obtain a relation between the degree of ionisation and the nature of the medium. This ionisation may, for mathematical convenience, be split into several auxiliary steps. In view of the results quoted in the preceding paragraph we assume that there is no storage of reagent at any intermediate stage and do not wish to imply that there need be any chemical significance in this breaking up of the thermodynamic equilibrium which must, of course, be independent of any assumed intermediate reaction path:

$$(1)\ H_2SO_4 \rightleftharpoons HSO_4^- + H^+$$
$$(2)\ R{\cdot}OH + H^+ \rightleftharpoons R{\cdot}OH_2^+$$
$$(3)\ R{\cdot}OH_2^+ \rightleftharpoons R^+ + H_2O$$

Let the equilibrium constants of these hypothetical steps be denoted by K_1, K_2, K_3, and the equilibrium constant of the overall equilibrium (I) by K_I. Then

$$K_I = K_1 . K_2 . K_3 = (R^+)(HSO_4^-)(H_2O)/(R{\cdot}OH)(H_2SO_4)$$

It follows from the definition of H_0 and of the related function h_0 ($H_0 = -\log_{10} h_0$), that

$$\frac{(HSO_4^-)}{(H_2SO_4)} = \frac{K_1}{h_0} . \frac{f_{R{\cdot}OH}}{f_{R{\cdot}OH_2^+}} = \frac{K_I}{(H^+)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where parentheses refer to activities and the f's are activity coefficients relative to the standard state of an infinitely dilute aqueous solution (Hammett, *loc. cit.*). Therefore

$$K_1 = \frac{(R^+)\,(H_2O)}{(R{\cdot}OH)} \cdot \frac{K_1}{k_0} \cdot \frac{f_{R{\cdot}OH}}{f_{R{\cdot}OH_2^+}}$$

and we may define a thermodynamic constant $K_{R{\cdot}OH}$ which will be a measure of the secondary basicity of R·OH:

$$K_{R{\cdot}OH} = K_1/K_1 = K_2{\cdot}K_3 = \frac{[R^+]}{[R{\cdot}OH]} \cdot \frac{(H_2O)}{k_0} \cdot \frac{f_{R^+}}{f_{R{\cdot}OH_2^+}} \quad . \quad . \quad . \quad . \quad . \quad (4)$$

We shall take $f_{R^+}/f_{R{\cdot}OH_2^+}$ as unity in all solvents considered, a step which is similar to Hammett's suggestion that all ratios of the form $\{f_{AH^+} \cdot f_B/f_{BH^+} \cdot f_A\}$ are approximately equal to unity, irrespective of the nature of A and B and of the solvent. This assumption is made by Hammett in the derivation of the H_0 function used in our treatment, and it is justified by the fact that the H_0 function has, within the limits of experimental error, a value independent of the indicator used. [It should be mentioned that Conant and Werner (*J. Amer. Chem. Soc.*, 1930, **52**, 4436) also recognised that the activity of water must be involved in this manner in the expression for the equilibrium constant of the ionisation of a triarylcarbinol in " superacid " solutions.] Taking logarithms and rearranging, we get

$$H_0 + \log (H_2O) = -pK_{R{\cdot}OH} + \log [R{\cdot}OH]/[R^+]$$

and this may be compared with the relation between the basicity constant K_b^B of an electrically neutral Brønsted base and the acidity function of the medium

$$H_0 = -pK_b^B + \log [B]/[BH^+] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

It is therefore suggestive to define an acidity function J_0, such that

$$J_0 = H_0 + \log (H_2O) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

$$= -pK_{R{\cdot}OH} + \log [R{\cdot}OH]/[R^+] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

which plays for the triphenylcarbinol type of ionisation (ionisation of an electrically neutral secondary base) a rôle analogous to that of the function H_0 for the ionisation of an electrically neutral Brønsted base. It is possible to define functions J_+, J_-, J_{++}, etc., given by $J_+ = H_+ + \log (H_2O)$, etc., to describe the potency of the solvent in inducing the ionisation of electrically charged secondary bases, the subscripts referring to the electrical charge of the base.

From our choice of the standard state [$(H_2O) \longrightarrow 1$, as solution $\longrightarrow H_2O$] it follows that as the medium composition tends to pure water, $J_0 \longrightarrow H_0$, which, in turn, under these conditions tends to the pH value.

Since the activity of water in the solvent, as defined above, is given by $(H_2O) = p/p^0$, where p and p^0 are the vapour pressures of water over the solvent and pure water, respectively, the J_0 scale is completely defined for any acid solution for which the H_0 function and the vapour pressure of water over the acid are known. This is so for nearly the whole of the composition range for H_2O–H_2SO_4 mixtures (vapour pressures: Hepburn, *Proc. Physical Soc.*, 1928, **40**, 247; Daudt, *Z. physikal. Chem.*, 1923, **106**, 225; Greenewalt, *Ind. Eng. Chem.*, 1925, **17**, 522; Collins, *J. Physical Chem.*, 1933, **37**, 1191; Shankman and Gordon, *J. Amer. Chem. Soc.*, 1939, **61**, 2370; Stokes, *ibid.*, 1947, **69**, 1291) and for an appreciable range for H_2O–$HClO_4$ mixtures (vapour pressures: Pearce and Nelson, *ibid.*, 1933, **55**, 3075). The J_0 scale calculated in this way for the system H_2SO_4–H_2O is tabulated in Table III, and the course of the function, along with that of the H_0 function, is plotted against the solvent composition in Fig. 7.

TABLE III.

The J_0 function for sulphuric acid–water mixtures at 25°.

H_2SO_4, %	H_0	$\log p/p^0$	J_0	H_2SO_4, %	H_0	$\log p/p^0$	J_0	H_2SO_4, %	H_0	$\log p/p^0$	J_0
5	+0·24	−0·01	+0·23	40	−2·28	−0·24	−2·52	70	−5·54	−1·37	−6·91
10	−0·16	−0·02	−0·18	45	−2·72	−0·33	−3·05	75	−6·16	−1·77	−7·93
15	−0·54	−0·04	−0·58	50	−3·23	−0·44	−3·67	80	−6·82	−2·28	−9·10
20	−0·89	−0·06	−0·95	55	−3·79	−0·58	−4·37	85	−7·62	−2·79	−10·41
25	−1·22	−0·08	−1·30	60	−4·32	−0·76	−5·11	90	−8·17	−3·49	−11·66
30	−1·54	−0·12	−1·66	65	−4·89	−1·03	−5·92	95	−8·74	−4·63	−13·37
35	−1·90	−0·17	−2·07								

Alternatively, the J_0 function could be experimentally determined by stepwise colorimetric or spectrophotometric measurements on indicators of the triphenylcarbinol type, analogously to Hammett's determination of the H_0 function by such measurements on Brønsted bases.

The correctness of these considerations may be tested in a limited way by plotting log ($[R^+]/[R{\cdot}OH]$) against J_0 [which according to equation (7) should give a straight line of *unit* slope] for a neutral indicator of the triphenylcarbinol type (4 : 4′ : 4″-trinitrotriphenylcarbinol) in sulphuric acid–water mixtures (Murray and Williams, *loc. cit.*; cf. Westheimer and Kharasch, *loc. cit.*). It is found (Fig. 8) that the points lie on a straight line of slope ~1·16. Although this agreement is not perfect, we believe that it is satisfactory, bearing in mind the not very high accuracy to which the H_0 scale is known. Any inaccuracy in this will, by our method of computing J_0, be imported into the J_0 scale. That such a degree of uncertainty in the H_0 scale is quite likely may be seen on plotting the logarithms of the ionisation ratios of several of Hammett and Deyrup's indicators covering the same range against one another. Lines of exactly unit slope are not always obtained, the discrepancies being considerably greater than ours in some cases. A plot of the logarithm of the indicator ratio for anthraquinone against that for 6-bromo-2 : 4-dinitroaniline (these being the only two indicators in Hammett and

FIG. 7.

Acidity functions of H_2SO_4–H_2O mixtures.

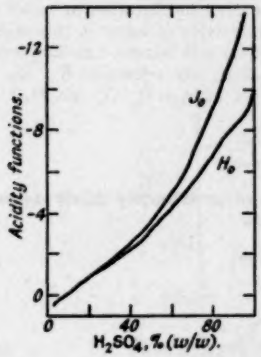
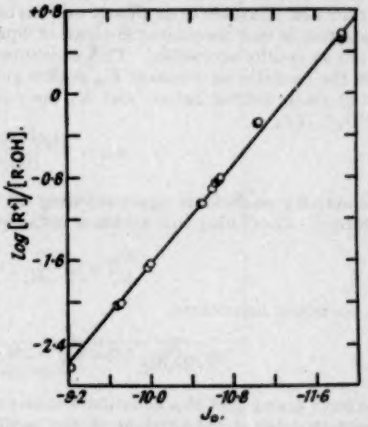


FIG. 8.

The dependence of the ionisation ratio for 4 : 4′ : 4″-trinitrophenylcarbinol upon the J_0 function.



Deyrup's work which cover the composition range to which the measurements on 4 : 4′ : 4″-trinitrotriphenylcarbinol relate) leads to a straight line of slope 1·08. The curious course of the H_0 function near 85% acid also suggests that the values in this region may require a slight revision. Therefore, while the behaviour of solutes in sulphuric acid still requires more detailed study, we would claim that the ionisation of triarylcarbinols is now as satisfactorily explained as the simpler basic ionisations in sulphuric acid.

From Fig. 8 it can also be deduced that $pK_{B\cdot OH}$ for 4 : 4′ : 4″-trinitrotriphenylcarbinol is ~11·4.* There have been earlier attempts to assess quantitatively the basicities of triarylcarbinols, particularly that of Baeyer and Villiger (*Ber.*, 1902, **35**, 3020). However, this work and most of the later investigations were based on an experimental method of doubtful value (cf. Ziegler and Boye, *Annalen*, 1927, **458**, 229) and lacked the understanding that halochromism in ketones and triphenylcarbinol was a manifestation of different kinds of basicity (see, however, Kolthoff, *J. Amer. Chem. Soc.*, 1927, **49**, 1218; Lund, *ibid.*, p. 1346).

The usefulness of the J_0 scale and of the basic dissociation constants obtainable with its aid may be illustrated with reference to the kinetics of aromatic substitution reactions. The

* Hammett prefers to record the strengths of weak bases in terms of the acidity constants of the conjugate acids, *i.e.*, the reciprocals of the basicity constants (or $pK_a^B = -pK_a^{BH^+}$). Since no such *simple* physical interpretation attaches to the reciprocal of the ionisation constant $K_{B\cdot OH}$ of a secondary base, it is not proposed to follow this practice.

second-order rate constant (k) for nitration by dilute solutions of nitric acid in aqueous sulphuric acid is related to the J_0 function by the equation

$$\log k = \log k_0 - J_0 - pK_{NO_2\cdot OH} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

where k_0 is a constant independent of the medium, and $K_{NO_2\cdot OH}$ is the ionisation constant of nitric acid as a secondary base, as defined by equation (4), provided that $[HNO_3] \gg [NO_2^+]$. From the intensities of Raman spectra of nitric acid in sulphuric acid (Chédin, *Ann. Chim.*, 1937, **8**, 295) it may be inferred that nitric acid (in low concentration) is half-ionised as a secondary base in ~88% sulphuric acid, and therefore that $pK_{NO_2\cdot OH}$ is ~11·2. Equation (8) is a slightly more exact statement of the treatment of aromatic nitration in aqueous sulphuric acid by Westheimer and Kharasch (*loc. cit.*) and, more particularly, by Lowen, Murray, and Williams (*J.*, 1950, 3318) where these considerations are elaborated. It is clear that with a more precise knowledge of the constant $K_{NO_2\cdot OH}$ it will be possible to obtain in a quantitative form the law for the diminution of nitration velocity in mixed acids containing more than ~90% of H_2SO_4, about which there has been considerable speculation (cf. Gillespie and Millen, *loc. cit.*). By studying acid-catalysed halogenations over a range of solvent composition for which the courses of H_0 and J_0 differ appreciably, it should be possible to decide whether halogenation is brought about by a halogen cation or the conjugate acid of the halogen hydroxide (cf. Derbyshire and Waters, *locc. citt.*).

III. *The Ionisation in Acid Media of Low Water Content.*—For solutions of triphenylcarbinol in mixtures of sulphuric and acetic acids with a very low concentration of water the ionisation is best considered in terms of equation (II), since the activity of water in this system is not so readily accessible. This ionisation may again be split up into several auxiliary steps, and the equilibrium constant K_{II} is then given by $K_{II} = K_1K_2K_3K_4$, the constants K_1, K_2, K_3 being those defined before, and K_4 the equilibrium constant for $H_2O + H_2SO_4 \rightleftharpoons H_3O^+ + HSO_4^-$; *i.e.*,

$$K_{II} = \frac{(H_3O^+)\,(HSO_4^-)^2}{(H_2SO_4)^2} \cdot \frac{[R^+]}{[R\cdot OH]} \cdot \frac{f_{R^+}}{f_{R\cdot OH}}$$

the activity coefficients again referring to the standard state of an infinitely dilute aqueous solution. Combining this equation with equation (3), we obtain

$$\frac{K_{II}}{K_1^2} = \frac{[R^+]}{[R\cdot OH]} \cdot \frac{[H_3O^+]}{h_0^2} \cdot \left(\frac{f_{H_3O^+} f_{R^+} f_{R\cdot OH}}{f^2_{R\cdot OH_2^+}}\right)$$

or, on taking logarithms,

$$\log \frac{[R^+]}{[R\cdot OH]} = \log \frac{K_{II}}{K_1^2} - 2H_0 - \log [H_3O^+] - \log\left(\frac{f_{H_3O^+} f_{R^+} f_{R\cdot OH}}{f^2_{R\cdot OH_2^+}}\right) \quad . \quad . \quad . \quad (9)$$

We have found that this equation assumes a useful form when the last term is taken to have a constant value ϕ independent of the medium—which is probably not introducing a serious error since it is symmetrical relative to the electrical charges and probably has a value close to zero—and $[H_3O]^+$ is replaced by the stoicheiometric concentration of water in the medium ($[H_2O]_{st.}$), which seems reasonable for very low concentrations of water. Therefore

$$\log [R^+]/[R\cdot OH] = \log K_{II}/K_1^2 - 2H_0 - \log [H_2O]_{st.} - \phi \quad . \quad . \quad . \quad . \quad (10)$$

Equation (10) has been tested by studying the variation of the ionisation ratio of triphenylcarbinol with changes of the H_0 function and the water concentration of the medium. It was found that, in sets of experiments in which the water content of the medium was kept constant and the acidity changed, the dependence of the ionisation ratio upon H_0 was twice as great as for a simple base. The dependence of the ionisation ratio upon the water concentration according to equation (10) is confirmed by the observation that all four sets of experiments, relating to different concentrations of added water, can fairly satisfactorily be represented on a single graph of $\log [R^+]/[R\cdot OH]$ against $(2H_0 + \log [H_2O]_{st.})$. This is shown in Fig. 9, where the straight line is drawn with a *theoretical slope* of -1. It must, however, be remarked that in order to bring the points of the set without deliberately added water into coincidence with the other sets it is necessary to assume a value for the residual moisture of the batch of acetic acid used in these experiments. (The water content of the sulphuric acid may be neglected in comparison.) In this way the value 0·032M. (0·055%) for the concentration of water in our " dry " acetic acid was found to give fair agreement, and this value is of the order of magnitude

to be expected from our purification method and criteria (cf. Experimental). All stoicheiometric water concentrations were therefore calculated by adding 0·032M. to the concentrations of deliberately added water.

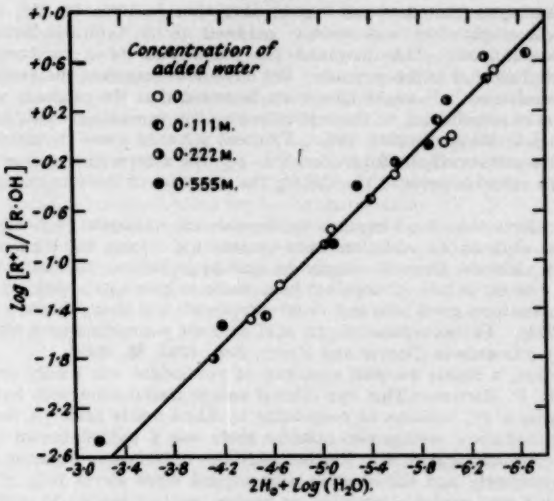
A more exact form of equation (10) must be used for media containing comparable amounts of added water and R·OH. In that case an appreciable second source of hydroxonium ions in the medium would be the ionisation of the triphenylcarbinol itself, and therefore, by modifying equation (10) we obtain

$$\log [R^+]/[R{\cdot}OH] = \log K_{II}/K_1^{\circ} - 2H_0 - \log \{[H_3O]_{st.} + [R^+]\} - \phi \quad . \quad . \quad . \quad (11)$$

It is doubtful if the region of validity of this equation can be investigated by using our technique and triphenylcarbinol as indicator, since the concentration of adventitious water in the

FIG. 9.

Test of equation (10).



hygroscopic medium is probably unavoidably large compared with the low concentration ($<10^{-4}$M.) of the indicator.

We thank Professor Gwyn Williams and Dr. M. A. Murray for giving us access to their data before publication. Our thanks are also offered to the Wiltshire County Education Committee for the award of a scholarship (to B. W. V. H.), and to the Research Fund of the University of London and to Imperial Chemical Industries Limited for grants for the purchase of apparatus.

KING'S COLLEGE, LONDON, W.C.2. [*Received, March 16th*, 1951.]

466. *Studies in Peroxidase Action. Part VI.** (a) *The Oxidation of* p-*Anisidine : a Further Example of Ready Demethoxylation.* (b) *Some Theoretical Considerations.*

By D. G. H. Daniels and B. C. Saunders.

The oxidation of *p*-anisidine by hydrogen peroxide in the presence of peroxidase at pH 4·5 is described. From the crude solid oxidation product, 2-amino-5-*p*-anisidinobenzoquinone di-*p*-methoxyphenylimine and tetramethoxyazophenine have been obtained crystalline. During the oxidation, the methoxyl group is eliminated as methyl alcohol.

Some suggestions for the mechanism of the peroxidase oxidation of amines are put forward.

In Part IV of this series (Saunders and Watson, *Biochem. J.*, 1950, **46**, 629) we reported that 4-methoxy-2 : 6-dimethylaniline was readily oxidised to 3 : 5-dimethylbenzoquinone 1-(4-methoxy-2 : 6-dimethyl)anil. This involved the elimination of a methoxyl group which appeared as methyl alcohol in the product. We have now examined the peroxidase oxidation of the simpler *p*-anisidine. It might have been expected that the products would have been exactly analogous in constitution to those obtained by the peroxidase oxidation of *p*-toluidine (Saunders and P. J. G. Mann, *J.*, 1940, 769). This was not so, nor was the reaction parallel with the oxidation of 4-methoxy-2 : 6-dimethylaniline, but the information gained with the latter substrate proved a valuable guide in elucidating the structure of the compounds obtained from *p*-anisidine.

There is no reference in the literature to the enzymic oxidation of *p*-anisidine. In fact, very little precise work on its oxidation, even by chemical means, has been recorded. Colorations with ferric chloride, chromic anhydride, and hypochlorous acid in acid solution have been mentioned, but no serious attempt has been made to investigate their nature. Bromine-water at low temperatures gives blue and violet compounds and then *p*-benzoquinone (Wieland, *Ber.*, 1910, **43**, 714). Peroxymonosulphuric acid oxidises *p*-anisidine to *p*-nitrosoanisole contaminated with *p*-nitroanisole (Baeyer and Knorr, *Ber.*, 1902, **35**, 3034).

For our reaction, a highly purified specimen of peroxidase was kindly supplied by Prof. Keilin and Dr. E. P. Hartree. This was diluted and in conjunction with hydrogen peroxide was used to oxidise a 2% solution of *p*-anisidine in dilute acetic acid. A deep violet colour was produced immediately, within two minutes there was a reddish-brown turbidity, and a red-brown solid gradually separated. Further additions of hydrogen peroxide and the enzyme were made intermittently and the reaction was stopped when about 70% of the *p*-anisidine had been converted into insoluble products, as further reaction tended to produce tar.

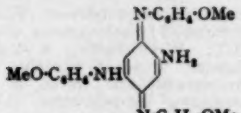
Ether dissolved 95% of the solid oxidation product. By chromatography of a benzene solution of the solid obtained on concentration of the solution, three compounds were isolated : (*a*) 4 : 4′-dimethoxyazobenzene in very small quantity ; (*b*) dark red needles, m. p. 236°, hereinafter called compound (II)—this represented 5% of the crude oxidation product ; (*c*) lustrous cerise-red leaflets, m. p. 164°, hereinafter called compound (I), and representing *ca.* 80% of the crude oxidation product.

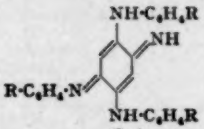
Elementary analysis and molecular-weight determination showed compound (I) to be $C_{27}H_{34}O_5N_4$, and determination of methoxyl groups and quantitative acetylation gave the partial formula $C_{24}H_{15}N_2(OMe)_3{\cdot}NH_2$. It thus appears that it is produced by condensation of four molecules of *p*-anisidine with the elimination of one methoxyl group. Hence, as we have previously obtained quinone anils by peroxidase oxidations, we suggest that compound (I) is 2-amino-5-*p*-anisidinobenzoquinone di-*p*-methoxyphenylimine, which has not previously been described. Quinone anils are often hydrolysed by mineral acids, but this did not occur in a simple manner with compound (I). With boiling dilute sulphuric acid, a complex mixture resulted, and with concentrated mineral acids an intense violet colour was produced, due presumably to the cation derived from (I).

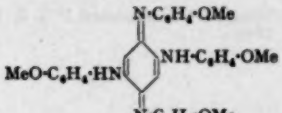
Elementary analysis and molecular-weight determinations showed compound (II) to be $C_{24}H_{22}O_4N_4$ which is derived from five *p*-anisidine residues with the elimination of one methoxyl and one amino-group. Moreover, it contained 4 methoxyl groups per mol. If the structure

* Part V, *J.*, 1950, 3519.

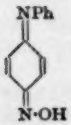
assigned to compound (I) is correct, then the most probable structure for (II) is 2 : 5-di-*p*-anisidinobenzoquinone di-*p*-methoxyphenylimine (or tetra-*p*-methoxyazophenine), *i.e.*, the NH_2 group of (I) is replaced by $NH{\cdot}C_6H_4{\cdot}OMe$. If so, then it should be possible to convert (I) into (II) by reaction with *p*-anisidine. This was found to be the case; the yield of compound (II) was good and ammonia was set free as expected.

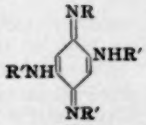

(I.)

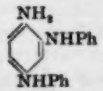

(Ia.)

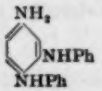

(II.)

Tetra-*p*-methoxyazophenine was first reported by Busch and Bergman (*Z. Farb. Text.*, 1905, **4**, 113), who prepared it by heating 4 : 4′-dimethoxydiazoaminobenzene, $MeO{\cdot}C_6H_4{\cdot}NH{\cdot}N{:}N{\cdot}C_6H_4{\cdot}OMe$, with *p*-anisidine and hydrochloric acid. They gave m. p. 242°. On repeating their work we found that the m. p. could not be raised above 236° even after repeated recrystallisations. However, the product which we obtained was identical with our oxidation product (II). This method of preparation does not demonstrate the structure unequivocally and we therefore sought an alternative and unambiguous synthesis of (II). Fischer and Hepp (*Ber.*, 1888, **21**, 667) heated together *p*-nitrosodiphenylamine [presumably acting in the tautomeric oxime form (III)], *p*-chloroaniline and hydrochloric acid, and obtained the trichloroazophenine (IV; R = Ph, R′ = C_6H_4Cl). On the other hand, using *p*-toluidine in place of *p*-chloroaniline, they obtained tetramethylazophenine (IV; R = R′ = C_6H_4Me) by a reaction in which the anil group must have been replaced by the *p*-toluidino-group (Fischer and Hepp, *Ber.*, 1887, **20**, 2480). By heating together *p*-nitrosodiphenylamine, *p*-anisidine, and hydrochloric acid we effected, in an analogous manner, the synthesis of a substance identical with our compound (II). The structures suggested above for (II) is thereby confirmed, and hence that of (I).


(III.)


(IV.)


(Va.)


(Vb.)

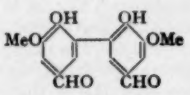
Precise Structure of Compound (I).—Compound (I) can alternatively be written in the imino-form (Ia; R = OMe). The structure of the corresponding compound (Ia; R = H) was discussed by Goldschmidt and Wurzschmitt (*Ber.*, 1922, **55**, 3226) who preferred (Ia) for two reasons: (i) its formation from *p*-quinone imine anil and aniline, (ii) loss of ammonia when hydrolysed by mineral acids. Reaction (i) proceeds presumably by the addition of aniline, oxidation of the resulting aminodianilinobenzene (Va and Vb) to a quinonoid compound, and repetition of the process. The fact that (ii) occurs only in the presence of mineral acid indicates that salt formation precedes hydrolysis. Thus in reactions (i) and (ii) an imino-group would in any case acquire a second hydrogen atom, *i.e.*, (I) and (Ia) are indistinguishable by the above chemical tests.

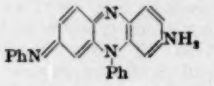
Discussion.—The following is a summary of peroxidase-catalysed reactions in which the products have been isolated and their structures elucidated.

Substrate.	Products.
Vanillin (Bourquelot and Marchadier, *Compt. rend.*, 1904, **138**, 1432)	Divanillin (VI)
Pyrogallol (Willstätter and Heiss, *Annalen*, 1923, **433**, 17)	Purpurogallin (for constitution see Barltrop and Nicholson, *J.*, 1948, 116; Haworth, Moore, and Pauson, *ibid.*, p. 1046)
o-Phenylenediamine [Chodat, Abderhalden's "Handbuch," 1925, (4), **1**, 319]	2 : 3-Diaminophenazine

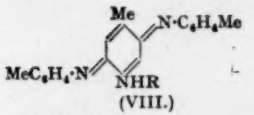
Substrate.	Products.
Catechol plus aniline (Pugh and Raper, *Biochem. J.*, 1927, **21**, 1378)	4 : 5-Dianilino-*o*-benzoquinone
Aniline (P. J. G. Mann and Saunders, *Proc. Roy. Soc.*, 1935, *B*, **119**, 47)	2 : 5-Dianilinobenzoquinone imine anil (I*a*, R = H), *pseudo*-mauvine (VII), indulines-3B and -6B, and aniline-black
p-Toluidine (Saunders and P. J. G. Mann, *J.*, 1940, 769)	4-Amino-2 : 5-toluquinone di-*p*-tolylimine (VIII; R = H), 4-*p*-toluidino-2 : 5-toluquinone di-*p*-tolylimine (VIII; R = C_6H_4Me), 4 : 4′-dimethyldiphenylamine, a small quantity of 4 : 4′-dimethylazobenzene, and traces of 4-amino-2 : 5-toluquinone 2-*p*-tolylimine (IX; R = H) and 4-*p*-toluidino-2 : 5-toluquinone 2-*p*-tolylimine (IX; R = C_6H_4Me)
p-Cresol (Westerfield and Lowe, *J. Biol. Chem.*, 1942, **145**, 463)	2 : 2′-Dihydroxy-5 : 5′-dimethyldiphenyl, the corresponding triphenyl, and a furan derivative
Mesidine (Chapman and Saunders, *J.*, 1941, 496)	3 : 5-Dimethylbenzoquinone 1-(2 : 4 : 6-trimethyl)-anil (X; R = Me)
Dimethylaniline (Naylor and Saunders, *J.*, 1950, 3519)	*NNN′N′*-Tetramethylbenzidine and its oxidation products
4-Methoxy-2 : 6-dimethylaniline (Saunders and Watson, *Biochem. J.*, 1950, **46**, 629)	3 : 5-Dimethylbenzoquinone 1-(4-methoxy-2 6-dimethyl)anil (X; R = OMe)
Mesitol (Booth and Saunders, *Nature*, 1950, **165**, 567)	2 : 6-Dimethylbenzoquinone and 4-hydroxy-3 : 5-dimethylbenzaldehyde

(VI.)

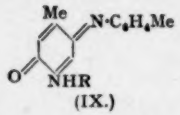




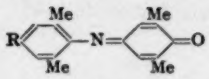
(VII.)



(VIII.)



(IX.)

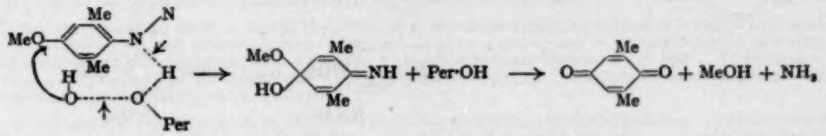


(X.)

Two points should be noted : (i) Primary amines give products mainly of the quinone imine type. A precursor of the general type $PhN{:}C_6H_4{:}NH$ (*o*- and *p*-) could account for these products by amine additions or hydrolysis. The possibility of such an intermediate has long been recognised (Goldschmidt and Wurzschmitt, *loc. cit.*). (ii) Robinson (*J.*, 1941, 220) has pointed out the close analogy between the oxidation of amines and phenols and the benzidine transformation, which is essentially a cationoid-type reaction (Dewar, " Electronic Theory of Organic Chemistry," p. 239). The oxidations may involve similar cationoid attack on the free amine or phenol. On the other hand, in instances where peroxidase products can also be obtained by inorganic oxidising agents there are no fixed requirements of pH, suggesting that neutral free radicals may be involved. These oxidations have usually been discussed on this basis in the past.

So far in this series of papers on peroxidase oxidation of amines, we have postulated two distinct radical intermediates : (i) $ArNH\cdot$ (or $ArN{:}$) formed by dehydrogenation (Saunders and P. J. G. Mann, *J.*, 1940, 769) and (ii) $HO\cdot$ derived from the hydrogen peroxide (Saunders and Watson, *Biochem. J.*, 1950, **46**, 629). The first kind was suggested by Goldschmidt (*Ber.*, 1920, **53**, 35), who oxidised ethereal solutions of amines by lead dioxide to compounds of the type $PhN{:}C_6H_4{:}NH$ and $PhN{:}NPh$. Coupling of the radicals in pairs could give rise to both these products, since the odd electron can be localised either on the nitrogen or on the *o*- and *p*-carbon atoms. If this kind of radical-coupling is a step in peroxidase oxidations, the almost complete absence of azo-compounds from the products is difficult to understand. The hypothesis that, under these conditions, the radical attacks an unchanged amine molecule would avoid this difficulty, since at any one moment (because of the low concentration of the catalyst) the primary dehydrogenation product must be surrounded by an excess of unchanged amine molecules. It is not clear whether such a resonance-stabilised radical possesses sufficient energy to do this.

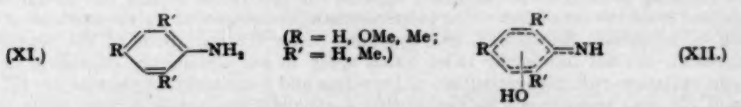
To explain the oxidation of 4-methoxy-2 : 6-dimethylaniline we have recently (Saunders and Watson, *loc. cit.*) suggested the second kind of mechanism. An activated complex containing the substrate and hydrogen peroxide could give rise to a quinone, ammonia, and methanol. It is noteworthy that, in this scheme, we can replace hydrogen peroxide by the secondary peroxidase–hydrogen peroxide complex, Per·OOH (cf. Chance, *Arch. Biochem.*, 1949, **22**, 224). The original enzyme Per·OH is then regenerated as follows :



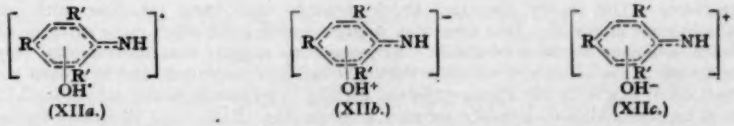
In this scheme it is not necessary to picture the HO radical as being free, *i.e.*, existing in a solution of hydrogen peroxide and peroxidase in the absence of substrate.

Proposed Generalised Scheme for Peroxidase Oxidation.—As it stands, the above scheme does not appear to be applicable to all cases, since it produces a quinone with at least one carbonyl group free, and it has been shown (Suida and Suida, *Annalen*, 1918, **416**, 134) that such quinones do not usually produce anils when they react with amines under mild conditions. The following modifications are suggested.

Let us assume that the oxidation of an aromatic amine (XI) takes place with simultaneous removal of a hydrogen atom and attachment of hydroxyl radical as in Saunders and Watson's

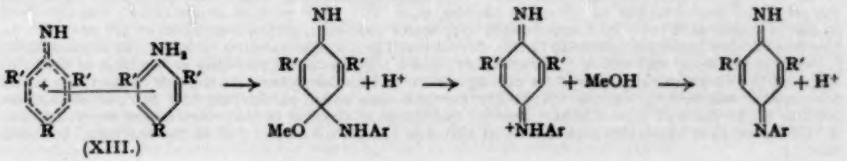


scheme. The resultant loose combination of the two radicals may be represented in the π-complex notation as (XII), of which the canonical forms are (XII, *a*, *b*, *c*). Of these, one would expect (XII*c*) to be favoured, especially when the amine carries substituents such as OMe (−*E*) which stabilise a cation. An anionoid replacement of the hydroxyl ion of this form by a molecule of unchanged amine, giving a new complex (XIII), should lead to a release of energy

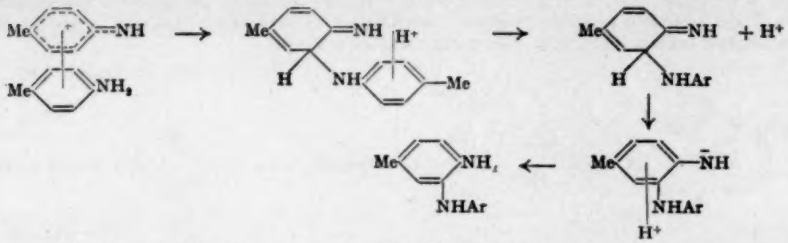


owing to the possibility of increased resonance. The NH^+ group in the cationoid half of this is of powerfully +*E* type; therefore there is likely to be attack upon the positions *ortho* and *para* to it by anionoid entities, and in particular by the anionoid half of the complex. The mode of rearrangement may vary according to the substituent present.

(i) R = OMe, R′ = Me or H. Here R can form a stable anion, so it undergoes simple replacement (cf. *p*-chloronitrobenzene and *p*-methoxynitrobenzene).



(ii) R = Me or H, R′ = H. Here neither R nor R′ can form a stable anion. Rearrangement leading to an aminodiphenylamine may occur. With *p*-toluidine, one of the *o*-positions will be attacked, as H has less $-I$ effect than Me:



The resultant aminodiphenylamine would undoubtedly have a lower oxidation–reduction potential than the parent amine, and thus would be readily oxidised to the quinoneimine anil assumed to be the precursor of the peroxidase products.

(iii) R = R′ = Me. Here, if the complex (XIII) is formed, the course of its rearrangement is obscure. If the *p*-methyl group is ejected as CH_3^- then methane should be produced: if as CH_3^+ then it might combine with HO^- to form methanol. This point (Chapman and Saunders, *J.*, 1941, 496) is not yet decided.

The complex (XIII) is identical with the one believed to be the essential intermediate in the rearrangement of hydrazobenzene to benzidine (Dewar, "Electronic Theory of Organic Chemistry," p. 237). It should be noted, however, that the benzidine rearrangement is carried out in reducing or indifferent conditions whereas the peroxidase system will favour electron withdrawal from the substrates. The relative potential energies of the orientations of (XIII) leading to benzidine, diphenyline, and semidine, under the conditions of the benzidine rearrangement, are not necessarily those which apply to our conditions. It should be noted that the oxidation–reduction potentials of benzidine and *p*-aminodiphenylamine are $E_0^{25} = 921$ mv. and 751 mv., respectively, indicating that *p*-aminodiphenylamine is more easily oxidised than benzidine. It must be emphasised that we are not suggesting that both these substances are actually produced, but rather that the orientations of (XIII) corresponding to these substances possess potential energies proportional to the above values of E_0^{25} under the prevailing oxidising conditions.

It is noteworthy that where aminodiphenylamine formation is prevented, as in the oxidation of dimethylaniline (Naylor and Saunders, *J.*, 1950, 3519), the oxidation product is a substituted benzidine.

Conclusion.—The theory discussed above depends upon ionic reactions, although free-radical steps are involved. This view may require modification when more experimental and theoretical evidence becomes available. At present we suggest that the essential steps are: (i) Formation of the secondary complex Per·OOH between peroxidase and hydrogen peroxide. (ii) Reaction of this with one amine molecule, leading to its simultaneous dehydrogenation and hydroxyl radical addition, possibly forming a π-complex (XII). (iii) Anionoid replacement of HO^- by a molecule of unchanged amine in favourable circumstances, giving the complex (XIII). (iv) Rearrangement of (XIII) to an *N*-aryl-quinone di-imine either directly or *via* an aminodiphenylamine. (v) Amine addition to the quinone di-imine if this is not sterically hindered, otherwise hydrolysis of the imino-group.

Experimental.

Oxidation of p-*Anisidine.*—The concentrated solution of peroxidase as supplied by Prof. Keilin and Dr. Hartree had an activity of 19·4 units/ml., and a P.N. of 1310. This was diluted with distilled water to an activity of 0·12 unit/ml. before use. Anisidine was distilled under reduced pressure and then recrystallised from benzene as colourless needles, m. p. 57°. The purified amine (10 g.) was dissolved in glacial acetic acid (11·5 ml.) and diluted with water (500 ml.), giving a solution of pH *ca.* 4·5. To this were added hydrogen peroxide (1 ml., 20-vol.) and peroxidase solution (4 ml.). An intense violet colour was produced and within 2 minutes there was a reddish-brown turbidity in the bulk of the solution, but the violet colour persisted for as long as 6 hours in isolated drops on the side of the flask, where the enzyme was in large excess. Hydrogen peroxide was added at the rate of 1 ml. per 45 minutes until in all 40 ml. had been added. Further quantities of enzyme (2 ml.) were added every 3 hours. A red-brown solid gradually separated and this was filtered off at the end of the reaction; its yield was 7 g.

Treatment of the Solid Oxidation Product.—The product (10 g.) was extracted in a Soxhlet apparatus successively with light petroleum (b. p. 40—60°), ether, ethanol, and acetone, the residue from one solvent being extracted by the next. The quantities removed by each solvent were respectively 0·1, 9·5, 0·3, 0·1 g. It was shown chromatographically that there was no significant difference in the composition of the light petroleum and ether extracts, so the former extraction was omitted in subsequent experiments.

Chromatography of the Ethereal Extract.—The ethereal extract was concentrated, and the solid which separated was dissolved in benzene and examined on alumina. The following principal bands were obtained: (*a*) yellow, (*b*) red, (*c*) brownish-red. Higher up the column, subsidiary bands appeared thus: (*d*) brown, (*e*) crimson, (*f*) pale violet, (*g*) brown, (*h*) brown, (*i*) black.

The lowest band (*a*) gave *ca.* 10 mg. (*i.e.*, from 10 g. of crude oxidation product) of a yellow substance of m. p. 145—160°, not obtained pure. However, it gave a red colour with concentrated sulphuric acid identical with that obtained with authentic 4 : 4′-dimethoxyazobenzene, m. p. 164°. Furthermore, a mixture of the yellow substance and 4 : 4′-dimethoxyazobenzene could not be separated into two components by chromatographic methods.

Compound (II).—Evaporation of band (*b*) gave a red solid which recrystallised from toluene as dark red needles, m. p. 235—236° (Found: C, 72·9; H, 5·62; N, 9·8; OMe, 21·0%; *M*, semimicro-ebullioscopic in ethylene dibromide, 590±30. Calc. for $C_{24}H_{22}O_4N_4$: C, 72·9; H, 5·71; N, 10·0; 4OMe, 22·1%; *M*, 560). The compound gave a violet colour, changing to blue on warming, with concentrated sulphuric acid, and could not be acetylated with acetic anhydride. Its mixed m. p. with authentic tetra-*p*-methoxyazophenine, prepared as described below, was 236°. A mixture of (II) and the authentic azophenine in benzene was not resolvable chromatographically on alumina.

Compound (I).—Evaporation of band (*c*) gave 2-*amino*-5-p-*anisidinobenzoquinone di*-p-*methoxyphenylimine*, lustrous cerise-red leaflets which, recrystallised from alcohol, had m. p. 164° (Found: C, 71·5; H, 5·76; N, 12·2; OMe, 20·4%; *M*, cryoscopic in ethylene dibromide, 450±25. $C_{31}H_{28}O_3N_4$ requires C, 71·3; H, 5·73; N, 12·33; 3OMe, 20·5%; *M*, 454). The compound gave an intense violet colour, changing to blue on warming, with concentrated sulphuric, hydrochloric, and nitric acids. It was recovered unchanged after treatment with 70% alcoholic sulphuric acid for 1 hour at room temperature, and tar resulted from boiling with 70% aqueous sulphuric acid. It was decolorised by reduction with zinc and acetic acid, the colour being rapidly restored by shaking with air.

Acetyl derivative. (*a*) The foregoing amino-compound was dissolved in excess of acetic anhydride and heated on a steam-bath for 10 minutes. The product solidified and the *acetyl* compound, recrystallised from acetone as dark red needles, had m. p. 213° (Found: C, 70·5; H, 6·02; N, 11·3. $C_{35}H_{30}O_4N_4$ requires C, 70·2; H, 5·64; N, 11·3%).

(*b*) The amino-compound (0·137 g.) was acetylated with a standardised mixture of acetic anhydride and pyridine, the excess of the anhydride being then titrated with 0·25N-sodium hydroxide solution. The quantity of acetic anhydride used in the acetylation was 0·036 g., and was thus equivalent to 1·1 ± 0·1 amino-groups per mol. The acetyl derivative from this experiment had m. p. 203—205° and was a slightly impure form of the acetyl derivative prepared as above.

Benzoyl derivative. Benzoylation could not be effected by the Schotten–Baumann method. When, however, the amino-compound was triturated with benzoyl chloride for 5 minutes in the cold and the excess of the acid chloride was removed with 10% sodium hydroxide solution, the *benzoyl* derivative was obtained; recrystallised from benzene as red-brown needles, it had m. p. 203—204° (Found: N, 10·6. $C_{34}H_{26}O_4N_4$ requires N, 10·0%).

Examination of the Filtrate from the Solid Oxidation Product.—The entire filtrate (3 l.) from the oxidation of 50 g. of *p*-anisidine was distilled through a Fenske column. A first fraction of 50 ml. (b. p. 98·5—99·5°) was collected. The presence of methanol in this solution was established as follows: (*a*) The solution (5 ml.) was mixed with potassium permanganate solution (2·5 ml.; 2%) and dilute sulphuric acid (5 ml.), and distilled into Schiff's reagent (5 ml.); a magenta coloration showed the production of formaldehyde. Control experiments without the solution, and with dilute methanol itself were carried out. (*b*) The solution (10 ml.) was mixed with sodium hydroxide solution (10 ml.; 10%) in a small mortar. Powdered 3 : 5-dinitrobenzoyl chloride (1 g.) was added, and the mixture ground together for 2 minutes, filtered off, and recrystallised from light petroleum; the m. p. and mixed m. p. with authentic methyl 3 : 5-dinitrobenzoate was 109°. (*c*) Methyl *p*-nitrobenzoate was similarly prepared, the m. p. and mixed m. p. with authentic specimen being 96°.

2 : 5-*Di*-p-*anisidinobenzoquinone Di*-p-*methoxyphenylimine*. *Tetra*-p-*methoxyazophenine*.—(*a*) 4 : 4′-Dimethoxydiazoaminobenzene (1·3 g.; prepared by Henriques's method, *Ber.*, 1892, **25**, 3064), *p*-anisidine (3 g., 5 mols.), and a few drops of concentrated hydrochloric acid were heated together at 100° for 9½ hours. The product was cooled and washed with water and then ethanol, and a residue (0·12 g.) of a dark red solid was left. This was recrystallised three times from toluene and had m. p. 235—236°, unchanged on admixture with compound (II) derived from the oxidation product.

(*b*) Pure *N*-nitrosodiphenylamine (34·5 g.) was subjected to the Fischer–Hepp transformation by passing dry hydrogen chloride into a suspension in alcohol. The *p*-nitrosodiphenylamine hydrochloride (32 g.) was obtained without first isolating the free base. An intimate mixture of the hydrochloride (3 g.) and *p*-anisidine (6 g.) was heated to 100° for 8 hours. The dark, tarry product was cooled and washed successively with water and ethanol, leaving a dark red crystalline residue (3·25 g., 43%). This azophenine was recrystallised four times from toluene and then had m. p., and mixed m. p. with compound (II) from the oxidation product, 235°. The synthetic azophenine and compound (II) were not separated when the benzene solution was subjected to chromatography on alumina.

Synthesis of Compound (II) *from Compound* (I).—An intimate mixture of compound (I) (0·45 g.), *p*-anisidine, and a few drops of concentrated hydrochloric acid was heated to 100° for 8 hours. After the cooled mass had been washed, a dark red solid was again obtained (0·34 g.; 60%), as described in the foregoing experiment. Recrystallised from toluene, it had m. p. 235°. The aqueous washings were made strongly alkaline with sodium hydroxide solution and, on warming, ammonia was evolved.

Our thanks are offered to the D.S.I.R. for a maintenance grant to one of us (D. G. H. D.), and we are grateful to Prof. Sir John Lennard-Jones, F.R.S., and to Dr. G. W. Kenner, with whom we have had valuable discussions.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, March 6th*, 1951.]

---

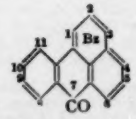
467. 1 : 8 : 9-*Naphthanthr*-10-*one*.

By WILLIAM BRADLEY and F. K. SUTCLIFFE.

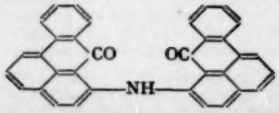
The fact that direct hydroxylation and amidation of *meso*benzanthrone yield only monosubstitution products is ascribed to neutralisation of the effect of the carbonyl group by hydroxyl and amino-substituents which conjugate with the nucleus, but derivation of a simple rule is complicated by the preference of anionoid reagents for either the *ortho*- or the *para*-position relative to the carbonyl group. In this connection 1 : 8 : 9-naphthanthr-10-one is interesting as it possesses two free positions *ortho* and two *para* to the carbonyl group; its direct hydroxylation affords a "*p*-" monohydroxy-derivative, the promoting effect of the carbonyl group being neutralised by the single hydroxyl substituent.

1 : 8 : 9-Naphthanthr-10-one affords a monobromo-derivative which resembles 3-bromo*meso*benzanthrone in yielding a blue quinonoid diketone when it is heated with alcoholic potassium hydroxide at 115—120°. 1 : 8 : 9-Naphthanthr-10-one, unlike *meso*benzanthrone, undergoes no change at this temperature, but fusion with potassium hydroxide at 240—250° affords a bluish-black quinonoid diketone resembling violanthrone. Further bromination of 1 : 8 : 9-naphthanthr-10-one yields a product approximating in composition to a dibromo-derivative. The constitutions of the monohydroxy-, monobromo-, and dibromo-derivatives are discussed, and those of the two isomeric quinonoid diketones.

ALTHOUGH *meso*benzanthrone (I) is preferentially halogenated and nitrated in the *Bz*-nucleus, direct replacement of hydrogen by hydroxy-, amino-, or piperidino-groups occurs at the 4- and 6-positions (Bradley, *J.*, 1937, 1091; 1948, 1175; Bradley and Jadhav, *J.*, 1937, 1791; 1948, 1622). By appropriate choice of conditions the monohalogenated *meso*benzanthrones can be further halogenated and nitrated (Cahn, Jones, and Simonsen, *J.*, 1933, 444; Nakanishi, *Chem. Abst.*, 1932, **26**, 4335) and the mononitro*meso*benzanthrones further nitrated (Pieroni, *Ann. Chim. appl.*, 1931, **21**, 155). When, however, the substituting agent is an anion the limit of substitution is the mono-derivative in the great majority of instances. For example, *meso*benzanthrone heated with potassium hydroxide and an oxidant affords 4- and 6-hydroxy*meso*benzanthrones (Perkin and Spencer, *J.*, 1922, 479; Bradley and Jadhav, *J.*, 1937, 1791), and direct amidation affords 6-amino*meso*benzanthrone and 6 : 6′-di*meso*benzanthronylamine (II), but polyamino-*meso*benzanthrones are not encountered (Bradley, *J.*, 1948, 1175). The result is expected because the effect of an *o*- or *p*-amino- or -hydroxyl substituent is to neutralise the effect of the carbonyl group on which the capacity for anion-substitutions depends.



(I.)



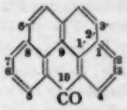
(II.)

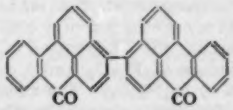
Monosubstitution by anions in aromatic compounds containing single cationoid substituents appears to be a common though not an invariable rule. Nitrobenzene affords a mixture of two monohydroxy-derivatives with potassium hydroxide (Wohl, *Ber.*, 1899, **32**, 3486; 1901, **34**, 2444) and mono-derivatives with potassiocarbazole (G. and M. de Montmollin, *Helv. Chim. Acta*,

1923, **6**, 94) and sodamide–piperidine (Bradley and Robinson, *J.*, 1932, 1254); α- and β-nitronaphthalenes behave similarly (Meisenheimer and Patzig, *Ber.*, 1906, **39**, 2533; Bradley and Robinson, *loc. cit.*).

When two cationoid groupings are present disubstitution products are commonly formed. Anthraquinone and potassium hydroxide yield alizarin; benzoquinone and aniline afford 2 : 5-dianilinobenzoquinone.

In considering the application of a rule relating the number of activating groups to the number of nuclear substitutions effected, account must be taken of the fact that most substituents preferentially enter either the *ortho*- or the *para*-position to the activating group. *meso*Benzanthrone yields 4-hydroxy- and 4-piperidino-*meso*benzanthrones but 6-amino- and 6-alkyl-*meso*benzanthrones. Nitrobenzene yields *o*-nitrophenol but *p*-nitrophenylcarbazole. Similarly, alkylquinolinium halides yield 1-alkyl-1 : 2-dihydro-2-hydroxyquinolines with alkali hydroxides (Decker, *Ber.*, 1892, **25**, 443, 3326), but 1-alkyl-4-cyano-1 : 4-dihydroquinolines with alkali cyanides (Kaufmann and Albertini, *ibid.*, 1909, **42**, 3776; Kaufmann and Widmer, *ibid.*, 1911, **44**, 2058). An opportunity to test the validity of such a rule occurs in 1 : 8 : 9-naphthanthr-10-one (III), a monoketone having two free positions *ortho* and two *para* to the carbonyl group, whose constitution permits disubstitution by anions unrestricted by considerations of preferred orientation.

(III.) 

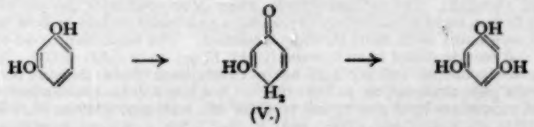


(IV.)

1 : 8 : 9-Naphthanthr-10-one was prepared by Scholl and Meyer (*Ber.*, 1930, **69**, 152) and by Vollmann, Becker, Corell, Streeck, and Langbein (*Annalen*, 1937, **531**, 155) who proved its constitution. Scholl and Meyer recorded the formation of dinitro- and dibromo-derivatives. In the present investigation it was found that 1 : 8 : 9-naphthanthr-10-one and bromine formed a dark, red-brown product, approximating in composition to $C_{19}H_{10}OBr_4$, which yielded 1 : 8 : 9-naphthanthr-10-one when heated with alcohol, pyridine, dilute aqueous sodium hydroxide or sodium hydrogen sulphite, but when kept or heated gave a dibromo-1 : 8 : 9-naphthanthr-10-one. Equimolecular amounts of bromine and 1 : 8 : 9-naphthanthr-10-one in hot nitrobenzene afforded a monobromo-derivative which for the reason given is considered to be the 3′-bromo-compound. The constitution of the dibromo-derivative was not determined but considerations of symmetry suggest that it is probably 3′ : 6′-dibromo-1 : 8 : 9-naphthanthr-10-one.

Unlike *meso*benzanthrone which yields 4 : 4′-di*meso*benzanthronyl (IV) when heated with alcoholic potassium hydroxide at 110° (Lüttringhaus and Neresheimer, *Annalen*, 1929, **473**, 259), 1 : 8 : 9-naphthanthr-10-one is unchanged by these reagents even at 125°, showing thus its lower reactivity towards substitution by anions. At 230—240°, 1 : 8 : 9-naphthanthr-10-one readily affords a monohydroxy-derivative when heated with manganese dioxide and potassium hydroxide, but more highly hydroxylated derivatives are not formed. The hydroxy-derivative resembles 4- and differs from 6-hydroxy*meso*benzanthrone in forming an acetate but not a boroacetate, in dissolving readily in aqueous sodium hydroxide, and in the yellow colour and green fluorescence of its aqueous alkaline solution. It is considered to be 2-hydroxy-1 : 8 : 9-naphthanthr-10-one. Under the conditions described 1 : 8 : 9-naphthanthr-10-one approaches *meso*benzanthrone in reactivity.

The absence of dihydroxy-derivatives shows clearly the ability of a hydroxyl substituent to neutralise the effect of a *para*-carbonyl substituent in promoting nuclear substitution by anions. The result harmonizes with the known formation of alizarin from either anthraquinone or 2-hydroxyanthraquinone by the action of alkali and an oxidant (Minaev and Fedorov, *Chem.*



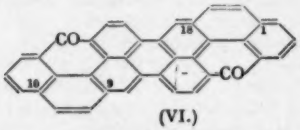
(V.)

Abs., 1929, **23**, 3701; Il'inski and Nikolayeva, Il'inski and Perelman, *ibid.*, 1937, **31**, 682; Graebe and Liebermann, *Annalen*, 1871, **160**, 130, 135; Liebermann, *ibid.*, 1876, **183**, 145, 169,

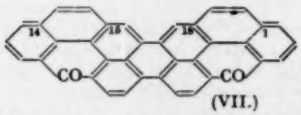
184, 203, 213; Baeyer and Caro, *Ber.*, 1874, **7**, 968, 972; Perkin *J.*, 1870, **23**, 133; 1874, **27**, 401), but it suggests that when trihydroxyanthraquinones result from the alkali fusion of dihydroxyanthraquinones additional carbonyl groups are formed at intermediate stages as a result of prototropic changes. Bradley and Robinson (*J.*, 1932, 1255) suggested that phloroglucinol was formed in the alkali fusion of resorcinol as a result of the hydroxylation of the keto-form (V), and the same process may account for the further hydroxylation of the dihydroxyanthraquinones.

Heated with alcoholic potassium hydroxide at 115—120°, 3′-bromo-1 : 8 : 9-naphthanthr-10-one affords a blue, halogen-free diketone having the properties of a quinone. It is insoluble in water or dilute aqueous sodium hydroxide, but it dissolves when sodium dithionite (hydrosulphite) is added. The absorption spectrum of a solution in concentrated sulphuric acid resembles that of *iso*violanthrone(*iso*dibenzanthrone). *iso*Violanthrone results when 3-bromo-*meso*benzanthrone is heated with alcoholic potassium hydroxide (Lüttringhaus and Neresheimer, *loc. cit.*), and the formation of a similar colouring matter from a monobromo-1 : 8 : 9-naphthanthrone suggests that the colouring matter is 9 : 10-18 : 1-bisbenz*iso*violanthrone (VI), and that the monobromo-1 : 8 : 9-naphthanthr-10-one is the 3′-bromo-derivative corresponding in structure to 3-bromo*meso*benzanthrone. It may be remarked that 3-bromo*meso*benzanthrone is the first product of bromination of *meso*benzanthrone as 3′-bromo-1 : 8 : 9-naphthanthr-10-one is of 1 : 8 : 9-naphthanthr-10-one.

According to Vollmann *et al.* (*loc. cit.*), heating 1 : 8 : 9-naphthanthr-10-one with alkali hydroxides results in the formation of a blue colouring matter. The present work has shown that the product contains the 2-hydroxy-1 : 8 : 9-naphthanthr-10-one recorded above, a bluish-black quinonoid diketone $C_{38}H_{16}O_2$, and a more highly oxidised substance the composition of which approximates to $C_{38}H_{18}O_6$. The diketone, although insoluble in warm dilute aqueous sodium hydroxide, dissolved sparingly in alkaline dithionite, forming a bluish-green solution. In concentrated sulphuric acid it gave a violet solution, the absorption spectrum of which differed from that of (VI) and resembled that of violanthrone. For these reasons the diketone is regarded as 14 : 15-18 : 1-bisbenzoviolanthrone (VII).



(VI.)



(VII.)

The third product, $C_{38}H_{18}O_6$, showed the properties of a quinone in that it dissolved in alkaline dithionite; its composition and quinonoid character suggest that it may be a tetrahydroxy-derivative of (VII).

Experimental.

Measurements of absorption spectra were made on a Barfit Hilger Nutting Spectrophotometer Type H. 410. The values of the extinction coefficients (*E*) are the readings on the scale of the instrument for 0·002% solutions in AnalaR sulphuric acid in a 2-cm. cell.

1 : 8 : 9-*Naphthanthr*-10-*one* (cf. Scholl and Meyer, *loc. cit.*).—Finely ground pyrene (200 g.; m. p. 148—149°) and then glycerol (320 c.c.) were added at 70—80° to a mixture of 95% sulphuric acid (2620 c.c.) and water (900 c.c.). The mixture was stirred for 3 hours on the steam-bath, then cooled and added to water (5 l.). The tarry precipitate was collected by decantation and stirred at 70—80° with water (4 l.), and 15% aqueous sodium hydroxide was added to permanent alkalinity. The residual brownish-yellow powder, collected, washed with water, and dried at 100° (114 g.), was then powdered finely and exhaustively extracted by acetone; the extract afforded 55 g. of brown crystals; these were dissolved at 100° in toluene (1 l.), and treated at that temperature with four successive 40-g. quantities of activated alumina, each being stirred in, filtered off, and washed with hot toluene (50 c.c.). The toluene solution, now pale, afforded orange-brown material (35 g.), m. p. 225—235°, on cooling. Two recrystallisations from boiling toluene (500 c.c.) gave orange-yellow needles (25 g.), m. p. 241—243° (Scholl and Meyer, *loc. cit.*, record m. p. 243°). The combined toluene mother-liquors were passed through a column of alumina. The chromatogram, when developed with the aid of toluene (500 c.c.), gave a broad orange-brown band of naphthanthr-10-one, a pale more mobile, yellow band, and a reddish-brown and a dark brown band, both more strongly adsorbed. The naphthanthr-10-one was eluted with toluene, recovered, and recrystallised from toluene (yield, 17 g.; m. p. 241—243°). The two portions of naphthanthr-10-one were united (42 g.) and again crystallised from toluene before use. Further crystallisation gave the pure material, m. p. 246—247°. A dilute solution in concentrated sulphuric acid was pink; it showed maximum light absorption at 4720° (*E*, 1·56) and 5540 A. (*E*, 0·58).

Oxidation. With chromium trioxide in 80% acetic acid 1 : 8 : 9-naphthanthr-10-one afforded 1 : 8 : 9-naphthanthronequinone as reported by Vollmann *et al.* (*loc. cit.*). No characteristic product resulted on oxidation with potassium permanganate in aqueous pyridine.

Bromination of 1 : 8 : 9-*Naphthanthr*-10-*one*.—(a) An excess of bromine added to a solution of naphthanthr-10-one in warm acetic acid produced a dark, reddish-brown precipitate; no hydrogen bromide was evolved. Recrystallisation of the product (m. p. 200—240°) from alcohol or pyridine, or warming with dilute sodium hydroxide solution, yielded unchanged naphthanthr-10-one.

(b) 3′-*Bromo*-1 : 8 : 9-*naphthanthr*-10-*one*. A solution of naphthanthrone (5 g.) and bromine (6·4 g.) in nitrobenzene (50 c.c.) containing carbon tetrachloride (0·5 c.c.) was heated under reflux for 2 hours. Hydrogen bromide was evolved and the liquid became almost colourless. On cooling, a dark brown solid separated (4·5 g.; m. p. 275—285°, after being washed with alcohol). The mother-liquors, steam-distilled, afforded material (2·4 g.), m. p. 240—253°. The two products were united and crystallised from toluene. The following fractions resulted: (A), m. p. 289—294° (2·6 g.); (B), m. p. 265—269° (1·4 g.); and (C), m. p. 200—250° (0·7 g.), consisting mainly of naphthanthr-10-one.

Fraction (A), stirred with chlorobenzene (500 c.c.), afforded a residue (m. p. 310—318°; 0·6 g.) and a solution. The latter was passed through a column of alumina, and the chromatogram was developed by chlorobenzene (600 c.c.) and, finally, chlorobenzene (500 c.c.) containing 0·5% of acetone. The main orange-yellow band was eluted by hot chlorobenzene (20 vols.)–methanol (1 vol.), and the product was recovered by concentration of the extracts. It separated as a yellow solid, m. p. 275—283° after shrinkage at 265°. It was combined with fraction (B) and stirred with toluene (500 c.c.), and the insoluble material (m. p. >300°; 0·5 g.) removed. The solution was passed through alumina and the chromatogram was developed by toluene (2 l.). The main band (yellow) was extracted (Soxhlet) by 200 c.c. of acetone–methanol (4 : 1 by vol.). On cooling, the filtered solution afforded yellow needles (1·7 g.), m. p. 272—274° (Found: C, 67·3; H, 2·6; Br, 25·6. Calc. for $C_{19}H_9OBr$: C, 68·5; H, 2·6; Br, 24·0%). The analytical results suggest that the product is a monobromonaphthanthr-10-one containing 9·4 mols. % of a dibromonaphthanthr-10-one. (Calc. for $0·906C_{19}H_9OBr + 0·094C_{19}H_8OBr_2$: C, 67·3; H, 2·5; Br, 25·4%). Further recrystallisation from *o*-dichlorobenzene raised the m. p. to 274—276° and increased the bromine content. (Found: Br, 28·2%). Redissolved in chlorobenzene and again chromatographed on alumina the material, m. p. 272—274°, was recovered by elution with acetone–methanol (4 : 1) unchanged in m. p. and bromine content (Found: Br, 25·8%). A dilute solution of the product in concentrated sulphuric acid was deep pink; absorption max. at 4830 (*E*, 1·58) and 5620 A. (*E*, 0·82).

(c) 1 : 8 : 9-Naphthanthr-10-one (0·404 g.), added to bromine (2 c.c.), reacted vigorously and dissolved. After 30 minutes the mass had become semi-solid. The whole was kept in a closed vessel over solid sodium hydroxide and under reduced pressure. The residual reddish-brown solid (0·746 g.) fumed slightly in air; it had an odour of bromine. Heated for 3 hours in an open vessel at 130° it became yellow (0·59 g.). This product was dissolved in chlorobenzene (250 c.c.), the solution passed through a column of alumina, and the chromatogram developed with chlorobenzene (500 c.c.). The broad orange band was eluted by hot chlorobenzene containing a small proportion of alcohol. Yellow needles, m. p. 440° (decomp.) (Found: Br, 31·0%), crystallised from the eluate on cooling. These appeared to consist mainly of a dibromo-1 : 8 : 9-naphthanthr-10-one (Calc. for $C_{19}H_8OBr_2$: Br, 38·9%). The product was added to excess of bromine, the solution left overnight, and the uncombined bromine volatilised by heat. The residue, recrystallised from chlorobenzene, again afforded yellow needles, m. p. above 440° (Found: Br, 43·7%). A dilute solution in concentrated sulphuric acid was bluish-pink; it exhibited absorption max. at 4930 (*E*, 1·06) and 5700 A. (*E*, 0·59).

2-*Hydroxy*-1 : 8 : 9-*naphthanthr*-10-*one*.—An intimate mixture of 1 : 8 : 9-naphthanthr-10-one (10 g.) with an equal weight of precipitated manganese dioxide was added during 10 minutes to a stirred melt of potassium hydroxide (60 g.) and water (6 c.c.) at 220—230°. The melt thickened and it became necessary to raise the temperature to 230—240° to maintain fluidity. After 1 hour at this temperature the black product was cooled, broken up, and then added to water (1 l.). The suspension was aerated at 80—90°, and the resulting fine, black undissolved powder was collected. It was then extracted four times at 80—90° with N-sodium hydroxide. The five alkaline solutions so obtained were acidified, each giving a gelatinous orange precipitate which was collected, washed, and dried. In each case the m. p. was 330—335° after a change from deep orange to yellow at *ca.* 270°; the successive yields were 0·58, 1·34, 0·27, 0·14, and 0·14 g.

The undissolved residue was suspended in dilute sulphuric acid, and the manganese oxide dissolved by sulphur dioxide. A yellow solid remained (7·3 g.; m. p. 247—251°). This was extracted thoroughly with hot benzene; the filtered extract afforded 6 g. of unchanged naphthanthr-10-one. The benzene-insoluble material (1·3 g.) was extracted twice by 0·25N-sodium hydroxide. The first extract, acidified, afforded 0·2 g. of material, m. p. 327—333°, the second extract only a trace of a precipitate. The alkali-insoluble residue was a dark brown, infusible solid (0·6 g.). The seven portions of alkali-soluble material were combined (2·7 g.) and heated under reflux with acetic anhydride (100 c.c.) containing boroacetic anhydride (from 2 g. of boric oxide). The resulting brown solution was filtered; brown crystals (2·4 g.) separated on cooling. These were almost completely soluble in chloroform (100 c.c.); after treatment of the filtered solution with charcoal and evaporation a yellow residue (2·3 g.; m. p. 230—231°) remained. Recrystallisation from acetic anhydride afforded yellow needles, m. p. 230—231° (1·9 g.).

The product (1·5 g.) was insoluble in aqueous sodium hydroxide; when boiled for 2 hours with 0·25N-sodium hydroxide (150 c.c.) it formed a yellow solution with a green fluorescence. Acidification afforded a gelatinous, brown precipitate which, collected, washed, and dried, yielded orange-yellow 2-*hydroxy*-1 : 8 : 9-*naphthanthr*-10-*one* (1·3 g.), m. p. 356—358°, unchanged by further recrystallisation from acetic acid (Found: C, 83·6; H, 3·7. $C_{19}H_{10}O_2$ requires C, 84·4; H, 3·7%). 2-Hydroxy-1 : 8 : 9-naphthanthr-10-one formed a deep yellow solution having a green fluorescence in concentrated sulphuric acid [absorption max. at 5110 A. (*E*, 1·44); min. at 5000 A. (*E*, 1·26)].

In parallel experiments 2-hydroxy-1 : 8 : 9-naphthanthr-10-one (0·1 g.) was heated under reflux for 30 minutes with (*a*) acetic anhydride (5 c.c.) and (*b*) acetic anhydride (5 c.c.) containing boroacetic anhydride (0·05 g.). On cooling, the two solutions deposited the same compound as orange needles, m. p. 230—231°, undepressed on admixture.

9 : 10-18 : 1-*Bisbenz*iso*violanthrone*.—3'-Bromo-1 : 8 : 9-naphthanthr-10-one (0·5 g.; m. p. 272—274°) was heated and stirred for 3 hours at 115—120° (inner temp.) with a solution containing potassium hydroxide (2·5 g.) and potassium acetate (0·25 g.) in ethanol (5 c.c.). The reactants became green immediately; within a few minutes the colour was dark olive-green, and at the end of the reaction blue-green in thin layers and black in bulk. When added to water (50 c.c.) which was then heated to boiling, the reaction product yielded an olive-green solid. This was washed with 1% aqueous sodium hydroxide and finally with water. The alkaline filtrates were orange, with a green fluorescence; acidification afforded only a trace of a pale brown precipitate. The alkali-insoluble material was dried and then extracted with boiling acetone; unchanged 3'-bromonaphthanthr-10-one (0·15 g.) dissolved. The residue was extracted with pyridine. A black substance dissolved which did not melt or dissolve in alkaline dithionite even with the addition of pyridine. The pyridine-insoluble product was a violet-black powder; in warm alkaline sodium dithionite solution containing 10% of pyridine it gave a deep bluish-green solution which was filtered, then aerated at 90—95°, and the precipitate solid was collected and washed with water. The iso*violanthrone* derivative was a violet-black powder (Found : C, 90·1; H, 3·4. $C_{32}H_{16}O_2$ requires C, 90·5; H, 3·2%), soluble in concentrated sulphuric acid with a deep bluish-green colour [absorption max. at 6370 (*E*, 1·41) and 7000 A. (*E*, 2·97)].

Alkali Fusion of 1 : 8 : 9-*Naphthanthr*-10-*one* : *Formation of* 2-*Hydroxy*-1 : 8 : 9-*naphthanthr*-10-*one and* 14 : 15-18 : 1-*Bisbenzoviolanthrone*.—1 : 8 : 9-Naphthanthr-10-one (5 g.; m. p. 243—245°) was stirred at 240—250° for 1·5 hours with a melt of potassium hydroxide (45 g.) and potassium acetate (5 g.). Whilst still molten the product was added to water (1 l.), and the suspension was heated on the water-bath, aerated for an hour, and then filtered. The bluish-black residue was washed several times with hot, dilute sodium hydroxide solution and finally with water. The alkaline filtrates were orange, with a strong green fluorescence. Acidification yielded a brown gelatinous precipitate and this was collected, washed, and dried. The product (0·4 g.), recrystallised from acetic acid, yielded 2-hydroxy-1 : 8 : 9-naphthanthr-10-one, m. p. 353—356°, not depressed by admixture with the compound prepared as above.

The alkali-insoluble bluish-black material (4·2 g.) was extracted for several hours with 1 : 2 : 4-trichlorobenzene–phenol (1 : 1), then filtered. There was a residue (A) (1·7 g.). The extract was concentrated to one-quarter bulk, then cooled, and a black solid (B) collected, washed with benzene, and dried (yield, 2·3 g.); this dissolved in concentrated sulphuric acid with a grey-green colour, in alkaline sodium dithionite with a pale blue colour, and in the same medium containing a small proportion of pyridine with a deep greenish-blue colour.

Fraction B (1 g.) was extracted by boiling trichlorobenzene (250 c.c.). An undissolved residue (0·3 g.) was removed by filtration and the hot filtrate was passed through a column of alumina at 160—170°. Development with boiling trichlorobenzene yielded a succession of bands. The most mobile was a pink band consisting mainly of naphthanthr-10-one. Further development with boiling trichlorobenzene containing 1% of cresols (mixed isomers) resulted in the elution of a pale blue band (solution D). Finally, boiling trichlorobenzene containing 2% of cresols was used; a pale brown band passed through the column, whilst a dark blue band occupied the uppermost one-third. The blue band was separated and the colouring matter eluted by trichlorobenzene–cresols (1 : 1 by vol.). The eluate, filtered, concentrated, and then mixed with toluene, deposited 14 : 15-18 : 1-*bisbenzoviolanthrone* as a blue-black powder (0·063 g.) (Found : C, 89·8; 89·4; H, 3·8, 3·3. $C_{32}H_{16}O_2$ requires C, 90·5; H, 3·2%). It formed in concentrated sulphuric acid a violet solution [absorption max. at 5320 (*E*, 1·76) and 7400 A. (*E*, 1·66)]. It dissolved sparingly in warm alkaline sodium dithionite solution with a bluish-green colour; in the presence of a small proportion of pyridine the intensity of the colour was greatly increased. The solution in hot trichlorobenzene or nitrobenzene was blue with a strong red fluorescence, which in more concentrated solutions almost masked the blue colour. The addition of a small quantity of phenol or cresol completely inhibited the fluorescence.

The by-product present in solution D was recovered by evaporation of the solvent and addition of acetone as a trace of blue-black material, soluble in concentrated sulphuric acid with a grass-green colour [absorption max. at 4880 (*E*, 1·12) and 7400 A. (*E*, 0·87)].

The residue (A) was a black powder, almost insoluble in boiling cresol, but soluble in a warm solution of sodium hydroxide (3 g.) and sodium dithionite (2 g.) in a mixture of water (180 c.c.) and pyridine (20 c.c.). The substance did not dissolve in the absence of pyridine. The solution was filtered and the filtrate aerated. A black precipitate formed and this *substance* was collected and washed (Found : C, 79·1; 79·4; H, 3·3, 3·6. $C_{34}H_{18}O_4$ requires C, 80·0; H, 3·2%). It dissolved in sulphuric acid forming a greyish solution [light absorption : ill-defined max. at 5700 (*E*, 1·0) and 6600 A. (*E*, 1·0)].

The authors thank the University of Leeds for the award of an I.C.I. Research Fellowship to one of them (F. K. S.).

THE CLOTHWORKERS' RESEARCH LABORATORY,
UNIVERSITY OF LEEDS.

[*Received, April* 19*th*, 1951.]

468. *The Addition of Thiolacetic Acid to Unsaturated Compounds.*

By R. Brown, W. E. Jones, and A. R. Pinder.

The reaction of thiolacetic acid with a variety of unsaturated compounds has been investigated. Addition products have been obtained in high yield, thiolacetic acid being in general a vigorous additive agent.

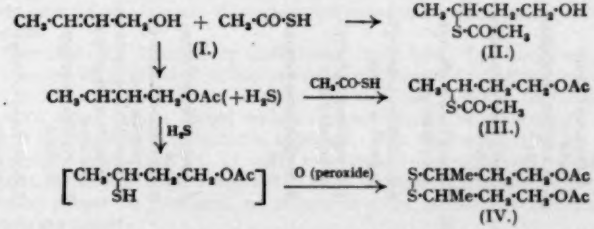
The investigations by Ipatieff and his co-workers (*J. Amer. Chem. Soc.*, 1938, **60**, 2731; 1939, **61**, 71) have shown that the direction of addition to asymmetrical olefinic hydrocarbons of the two fragments produced by scission of the S–H bond in a thiol may be "normal" or "abnormal" with respect to Markownikoff's rule. "Normal" addition occurred in the presence of acids, whereas in the absence of catalysts "abnormal" addition was observed. Jones and Reid (*ibid.*, 1938, **60**, 2452) and Kharasch, Read, and Mayo (*Chem. and Ind.*, 1938, **16**, 752) found that traces of peroxides catalysed "abnormal" addition very strongly.

Thiolacetic acid has been studied as an additive agent by a number of workers. Holmberg (*Arkiv Kemi, Min., Geol.*, 1938, **12**, B, No. 47) obtained 2-phenylethyl thiolacetate by "abnormal" addition of the acid to styrene, and Ipatieff and Friedman (*J. Amer. Chem. Soc.*, 1939, **61**, 71) showed that the addition of thiolacetic acid to a series of aliphatic olefins was "abnormal" in character. More recently, Cunneen (*J.*, 1947, 134) has investigated the addition to cyclic olefins and rubber (cf. U.S.P. 2,419,943, 2,420,194). 3-Chloropropyl thiolacetate was obtained by Sjöberg (*Ber.*, 1941, **74**, 64) by addition of thiolacetic acid to allyl chloride, and addition of the acid to αβ-unsaturated carboxylic acids has been reported by Holmberg and Schjånberg (*Ber.*, 1941, **74**, 1751), Reppel (U.S.P., 2,408,095) and Owen and his co-workers (*J.*, 1947, 1030; 1949, 3105, 3109). Catch, Cook, Graham, and Heilbron (*J.*, 1947, 1609) have found that simple αβ-unsaturated aldehydes react additively with thiolacetic acid. In the majority of cases, addition occurred readily, and the thiolacetates were obtained in high yield. In additions to αβ-unsaturated carbonyl compounds, the thiolacetate group invariably appeared at the β-carbon atom.

The present work, carried out in 1944 and 1945 in connexion with investigations in the penicillin field, describes the addition of thiolacetic acid to some unsaturated hydrocarbons, aldehydes, ketones, alcohols, and esters, in the presence of added peroxide.

The addition of thiolacetic acid to olefinic hydrocarbons occurred exothermically and with great ease (cf. Cunneen, *loc. cit.*). Oct-1-ene and hexadec-1-ene gave high yields of, respectively, *n*-octyl and *n*-hexadecyl thiolacetate, the "abnormal" products. Hydrolysis furnished the corresponding thiols, characterised as the 2 : 4-dinitrophenyl sulphides. With oct-2-ene, a quantitative yield of a product presumed to be a mixture of 2- and 3-acetylthio-*n*-octane was obtained. Thiolacetic acid and α-methylstyrene gave in high yield a product almost certainly resulting from "abnormal" addition, *i.e.*, 2-phenyl-*n*-propyl thiolacetate.

Acraldehyde and crotonaldehyde reacted readily with thiolacetic acid to give β-acetylthiopropaldehyde and -*n*-butaldehyde, respectively. These products were characterised as their 2 : 4-dinitrophenylhydrazones, which were identical with products of proved structure obtained by Catch, Cook, Graham, and Heilbron (*loc. cit.*). With cinnamaldehyde was obtained an addition product to which has been assigned the formula of β-acetylthio-β-phenylpropaldehyde, by analogy. High yields of addition products were also obtained with mesityl oxide and benzylideneacetone; it is almost certain that the thiolacetate group is at $C_{(\beta)}$, in the light of previous experience.



The addition of thiolacetic acid to allyl alcohol gave an almost quantitative yield of 3-acetylthio-*n*-propanol which, on hydrolysis, furnished 3-mercapto-*n*-propanol, identified as

Additive reactions of thiolacetic acid.

Unsaturated compound.	Product.	B. p., etc.	Yield, %	Formula.	S, %. Found.	S, %. Reqd.	Derivative.	Formula.	Found, %.	Reqd., %.
α-Methylstyrene	2-Phenyl-*n*-propyl thiolacetate	105°/4 mm. n_D^{20} 1·5429	90	$C_{11}H_{14}OS$	16·6	16·5	2-Phenyl-*n*-propanethiol; b. p. 74°/1 mm.; n_D^{20} 1·5510	$C_9H_{12}S$	S, 21·3	S, 21·05
Oct-1-ene	*n*-Octyl thiolacetate	132—133°/23 mm. n_D^{20} 1·4648	100	$C_{10}H_{20}OS$	17·4	17·0	2 : 4-Dinitrophenylthio-*n*-octane; plates, m. p. 78° [1]	$C_{14}H_{20}O_4N_2S$	N, 8·9	N, 9·0
Oct-2-ene	2- and 3-Acetylthio-*n*-octane	123—126°/28 mm.	100	$C_{10}H_{20}OS$	17·4	17·0	*n*-Octane-2- and -3-thiol; b. p. 92°/36 mm.	$C_8H_{18}S$	S, 21·9	S, 21·5
Hexadec-1-ene	*n*-Hexadecyl thiolacetate	168°/1·5 mm. m.p. 30·5°	75	$C_{18}H_{36}OS$	10·0	10·7	2 : 4-Dinitrophenylthio-*n*-hexadecane; plates, m. p. 91° [2]	$C_{22}H_{36}O_4N_2S$	N, 6·4	N, 6·6
Acraldehyde	β-(Acetylthio)propaldehyde [3]	66—70°/1 mm. n_D^{20} 1·5079	65	$C_5H_8O_2S$	24·1	24·2	2 : 4-Dinitrophenylhydrazone; yellow needles, m.p. 128° [4]	$C_{11}H_{12}O_6N_4S$	C, 42·4 H, 3·9 N, 17·9	C, 42·3 H, 3·85 N, 17·9
Crotonaldehyde	β-Acetylthio-*n*-butaldehyde [5]	59—60°/2 mm. n_D^{20} 1·5025	100	$C_6H_{10}O_2S$	22·8	21·9	2 : 4-Dinitrophenylhydrazone; golden prisms, m. p. 95° [6]	$C_{12}H_{14}O_6N_4S$	C, 44·9 H, 4·4 N, 17·5	C, 44·2 H, 4·3 N, 17·2
Cinnamaldehyde	β-Acetylthio-β-phenylpropaldehyde	115—117°/1 mm. m. p. 44°	90	$C_{11}H_{12}O_2S$	15·3	15·4	2 : 4-Dinitrophenylhydrazone; yellow needles, m. p. 145°	$C_{17}H_{16}O_6N_4S$	C, 53·1 H, 4·2 N, 14·5	C, 52·6 H, 4·1 N, 14·4
Mesityl oxide	4-Acetylthio-4-methyl-*n*-pentan-2-one	84—86°/6 mm.	92	$C_8H_{14}O_2S$	18·4	18·4	2 : 4-Dinitrophenylhydrazone; orange-red prisms, m. p. 83—84°	$C_{14}H_{18}O_6N_4S$	C, 47·7 H, 5·0 N, 15·6	C, 47·5 H, 5·1 N, 15·8
Benzylideneacetone	4-Acetylthio-4-phenyl-*n*-butan-2-one	m. p. 67—68°	90	$C_{12}H_{14}O_2S$	13·8	14·4	2 : 4-Dinitrophenylhydrazone; orange-red prisms, m. p. 128—129°	$C_{18}H_{18}O_6N_4S$	C, 54·4 H, 4·4 N, 14·0	C, 53·7 H, 4·5 N, 13·9
Allyl alcohol	3-Acetylthio-*n*-propan-1-ol	72—75°/1·5 mm. n_D^{20} 1·4827	97	$C_5H_{10}O_2S$	23·9	23·9	*p*-Nitrobenzoate; plates, m. p. 76°	$C_{12}H_{13}O_5NS$	C, 51·3 H, 4·7 N, 5·1	C, 50·9 H, 4·6 N, 5·0
							3-Mercapto-*n*-propanol bis-α-naphthylurethane, needles, m. p. 174—175° [7]	$C_{25}H_{25}O_3N_2S$ [8]	N, 6·8	N, 6·5
Crotyl alcohol	3-Acetylthio-*n*-butan-1-ol	85°/15 mm. n_D^{20} 1·4605	55	$C_6H_{12}O_2S$	21·5	21·6	—	—	—	—
2-Methylallyl alcohol	3-Acetylthio-2-methyl-*n*-propan-1-ol	121—122°/23 mm. n_D^{20} 1·4856	77	$C_6H_{12}O_2S$	21·7	21·6	—	—	—	—
Eugenol	3′-Acetylthio-4-hydroxy-3-methoxy-*n*-propylbenzene	180°/1·5 mm.	78	$C_{12}H_{16}O_3S$	13·1	13·3	Benzoate; prisms, m. p. 80—81°	$C_{19}H_{20}O_4S$	C, 66·0 H, 6·0 S, 9·4	C, 66·3 H, 5·8 S, 9·3
Allyl acetate	3-Acetylthio-*n*-propyl acetate	125°/24 mm. 90°/4 mm. n_D^{20} 1·4720	100	$C_7H_{12}O_3S$	18·3	18·2	3-Mercapto-*n*-propanol bis-α-naphthylurethane, needles, m. p. 174—175° [7]	$C_{25}H_{25}O_3N_2S$	N, 6·8	N, 6·5
Crotyl acetate	3-Acetylthio-*n*-butyl acetate	110°/11 mm. n_D^{20} 1·4674	74	$C_8H_{14}O_2S$	16·5	16·8	—	—	—	—
2-Methylallyl acetate	3-Acetylthio-2-methyl-*n*-propyl acetate	133—134°/24 mm. n_D^{20} 1·4693	80	$C_8H_{14}O_2S$	16·8	16·8	—	—	—	—
Cinnamyl acetate	3-Acetylthio-3-phenyl-*n*-propyl acetate	124—130°/1 mm. n_D^{20} 1·5292	38	$C_{13}H_{16}O_2S$	13·2	12·7	—	—	—	—
Maleic anhydride	(Acetylthio)succinic anhydride	m. p. 76—77°	83	$C_6H_6O_4S$ [9]	18·6	18·4	—	—	—	—

[1] Bost, Turner, and Norton, *J. Amer. Chem. Soc.*, 1932, **54**, 1985, give m. p. 78°. [2] *Idem, ibid.*, give m. p. 91°. [3] Catch, Cook, Graham, and Heilbron, *J.*, 1947, 1610, give b. p. 92—93°/14 mm., yield 68%. [4] *Idem, ibid.*, give m. p. 127·5°. [5] *Idem, ibid.*, give b. p. 91—92°/11 mm. and yield 65%. [6] *Idem, ibid.*, give m. p. 96°. [7] Undepressed on admixture with an authentic specimen, m. p. 174—175°. [8] Found: C 41·8; H, 3·6. Calc.: C, 41·4; H, 3·45%.

its bis-α-naphthylurethane. Allyl acetate behaved in a similar manner. Crotyl alcohol (I) gave a product presumed by analogy to be 3-acetylthio-*n*-butan-1-ol (II), together with (probably) the acetate of this product (III) and the disulphide (IV). The formation of these substances is envisaged on page 2123.

Addition products, probably of analogous structure, have also been obtained in good yield with 2-methylallyl alcohol, eugenol, crotyl acetate, and 2-methylallyl acetate, but with cinnamyl acetate a poor yield was afforded. No addition was observed to occur with cinnamyl alcohol and stilbene (cf. Posner, *Ber.*, 1905, **38**, 646).

The results are summarised in the Table.

Experimental.

Preparation of Thiolacetates.—The following are typical reaction conditions. Thiolacetic acid (1—2 mols.) was added dropwise, with shaking and cooling, to a mixture of the unsaturated compound (1 mol.) and ascaridole (few drops) or benzoyl peroxide (few mg.). In some cases reaction was immediate; in others the reaction was completed by heating the solution under reflux on the water-bath for several hours. The mixture was worked up by fractional distillation *in vacuo*. In a few cases the reaction product crystallised, and was collected and recrystallised from a suitable solvent.

Characterisation of Thiolacetates.—Hydrolysis of the thiolacetates was effected by boiling with aqueous potassium hydroxide. The thiols so obtained were characterised as their phenyl- or α-naphthylurethanes, or as their condensation products with chloro-2 : 4-dinitrobenzene. Aldehydic and ketonic thiolacetates were characterised as their 2 : 4-dinitrophenylhydrazones. Alcoholic products were converted into the benzoate or *p*-nitrobenzoate.

Addition of Thiolacetic Acid to Crotyl Alcohol.—Crotyl alcohol (50 g.), thiolacetic acid (53 g.), and ascaridole (5 drops) were mixed and kept overnight, and then heated under reflux on the water-bath for 2 hours. Fractionation gave three products: (i) 57 g. of *3-acetylthio-*n*-butan-1-ol*, b. p. 85°/15 mm., n_D^{20} 1·4605 (Found: S, 21·5. $C_6H_{12}O_2S$ requires S, 21·6%); (ii) 20 g. of *3-acetylthio-*n*-butyl acetate*, b. p. 90°/4 mm. (Found: S, 16·7; Ac, 45·2. $C_6H_{14}O_2S$ requires S, 16·8; Ac, 45·3%); (iii) 10 g. of *bis-3-acetoxy-1-methyl-*n*-propyl disulphide*, b. p. 158°/3 mm. (Found: S, 22·2; Ac, 31·9. $C_{12}H_{22}O_4S_2$ requires S, 21·8; Ac, 29·3%).

The authors thank Miss D. E. Lofthouse for assistance, and the Chief Scientific Officer, Ministry of Supply, for permission to publish this work.

Research Establishment, Sutton Oak, St. Helens, Lancs. [*Received, March 5th*, 1951.]

---

469. *The Determination of Water in Pyridine Homologues by the Use of Infra-red Spectroscopy.*

By E. A. Coulson, J. L. Hales, and E. F. G. Herington.

Published methods for the determination of water in pyridine homologues are reviewed briefly. An infra-red spectroscopic procedure is given which allows water concentrations down to 0·002% v/v to be determined rapidly and requires only 0·1 ml. of the base. A drying technique suitable for use in the measurement of the true zero absorption of these bases in the absence of water is described.

During the preparation of highly purified samples of the bases, pyridine, α-, β-, and γ-picoline, and 2 : 6-lutidine, it was realised that water was likely to be the major residual impurity. The ratio of the molecular weights of water to base are roughly 1 : 5 for this series of compounds so that 0·02% v/v of water corresponds to 0·1 mol. per cent. of impurity, and the presence of a small amount of water on a volume basis is of considerable importance when purities are expressed as a molar percentage.

"AnalaR Standards for Laboratory Chemicals," 2nd Edn., London, 1927, describes an acceptance test for pyridine founded on the presence or absence of cloudiness when 5 ml. of the base are mixed with 5 ml. of carbon disulphide. We find that pyridine containing as much as 6% by volume of water can be mixed with an equal volume of carbon disulphide and no cloudiness due to the separation of water is apparent. But on the other hand, if a sample of pyridine containing no more than 1% of water by volume is admixed with twice its volume of carbon disulphide cloudiness readily appears. With pyridine containing less than 0·25% of water a cloudiness cannot be produced, no matter in what ratio the volumes of sample and carbon disulphide are mixed.

A method which depends on the titration of the acid produced when acetic anhydride reacts with pyridine has been described by Pesez (*Ann. Pharm. franç.*, 1946, **4**, 98), but this requires

5 ml. of pyridine and is only suitable for solutions containing more than a few tenths per cent of water.

The Karl Fischer reagent (see " Aquametry " Mitchell and Smith, Interscience Publishers, New York, 1948, for a summary) can be used for determining fairly small concentrations of water, but the large quantities of pyridine required (of the order of 100 ml.) when the water content is low makes the method not so convenient as that to be described, while in this laboratory percentages of water less than 0·01% have been found to be difficult to determine with this reagent.

The method described here is based upon the qualitative observations of Bosschieter, Errera, and Gaspart (*Physica*, 1938, **5**, 115) that the height of the absorption band near 3450 cm.$^{-1}$ in the infra-red spectrum of pyridine depends upon the water concentration. The published curves show a small band in the spectrum of pyridine and in the spectra of mixtures containing 1, 6, and 12% of water. The authors attribute the band to the formation of a hydrogen bridge between the nitrogen atom of the pyridine and the water molecule.

In view of the difficulty we have experienced in obtaining and maintaining pyridine in a dry state it was decided to prepare a new specimen in order to confirm that pyridine itself has an absorption band near 3450 cm.$^{-1}$. We found this band at 3420 cm.$^{-1}$, and the measured absorption of a dry specimen at this wave number was used as the true zero absorption; water was then added in known amounts and the dependence of the height of the absorption band on water concentration established. The experiments were extended to the picolines and 2 : 6-lutidine, and it was found that 0·002% v/v of water was detectable in all these bases and that this figure also represented the uncertainty in the determined water content up to 0·05% water, when a cell 1-mm. thick was used.

Experimental.

The base samples employed have been prepared at the Chemical Research Laboratory and details of the preparation will be described in another paper. For the present purposes it suffices to state that no absorption bands other than that of the base under study, and water if present, were detectable.

All spectroscopic measurements were carried out on a Hilger D.209 double-beam infra-red spectrometer a rocksalt prism being used. For a description of the instrument and a discussion of the accuracy of the wave-number calibration ($\pm$15 cm.$^{-1}$ in the range 5000—2000 cm.$^{-1}$ (see Hales, *J. Sci. Instr.*, 1949, **26**, 359). The transmission of the cells used was determined with carbon tetrachloride which has a high transmission at 3420 cm.$^{-1}$.

The efficacy of various drying techniques was followed by measuring the absorption band at 3420 cm.$^{-1}$. Müller (*Sitzungsber. Akad. Wiss. Wien*, 1922, **131**, 19) has described a drying method based on electrolysis between platinum electrodes, but this was found to be very slow with pyridine with the result that, unless very special precautions were taken, water was picked up more quickly than it was removed.

Several amalgams were tried as drying agents but the main disadvantage of most of these was the slowness of the reaction. Solid sodium amalgam was found to remove water fairly rapidly but the well-known chemical reaction of sodium with pyridine quickly produced a coloration of the liquid and the appearance of a broad absorption band almost coincident with the water association band.

Distillation of a sample of pyridine containing 0·25% v/v of water from baryta had no effect on the water content.

Fractional freezing proved to be effective for the removal of water from β-picoline (m. p. $-18°$) although the water content could not be reduced below 0·02% v/v, as subsequently measured by the technique described below. The water content of pyridine was not reduced below 0·05% v/v by fractional freezing, probably as a consequence of the difficulty of manipulating this dry base sample at low temperatures.

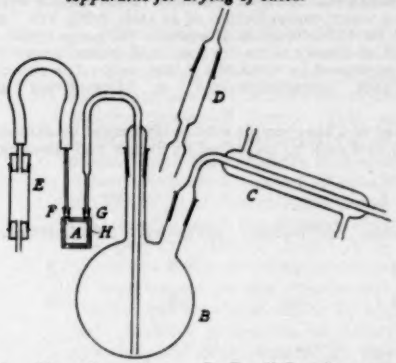
Azeotropic distillation of pyridine with benzene has been recommended as a method of reducing the water content below 0·01% (see " Aquametry," p. 67). In our experience it is difficult to remove traces of benzene from the pyridine by this procedure without the use of an efficient fractionating column, whilst if a good column is used the rate of distillation is so slow that recontamination of the pyridine with water presents a real hazard.

Pyridine forms a minimum-boiling azeotrope with water, and this may be used to dry a base sample by straight distillation without the addition of an entrainer. It was found that during the transference of dried pyridine to the spectrometer absorption cell by means of a pen-filler type of pipette water was picked up from the atmosphere to an extent corresponding approximately to 0·02% v/v. The apparatus shown in Fig. 1 was therefore constructed in order that the absorption cell (1 mm. thick) could be filled directly from the distillation flask. The dimensions of the apparatus were such that the whole equipment could be accommodated within the spectrometer.

In all the examples described below, initially approximately 300 ml. of the pyridine homologue were taken and were distilled into a graduated cylinder through *C* whilst a slow stream of dry air was passed *via* the phosphoric oxide tube *E* and through the liquid in *B*. This air current prevented the base from entering the absorption cell *A*, assisted boiling in *B*, and prevented the diffusion of atmospheric moisture into *B* through *C*. When it was decided to make a spectral measurement the distillation was discontinued, the condenser *C* was disconnected, and the joint immediately stoppered with the phosphoric oxide

tube *D*, after which the current of dried air was turned off. Suction was applied through *E*, the liquid drawn over into *A* from the flask *B*, and a spectral measurement made. The cell was emptied and refilled for a second spectral measurement by applying suction through *D* and *E*, respectively. The cell *A* was flushed with liquid before filling it for each spectral determination.

FIG. 1.
Apparatus for drying of bases.



A. *Absorption cell.* *D, E.* P_2O_5 *tubes.*
B. *Distillation flask.* *F, G.* *Hypodermic needles.*
C. *Condenser.* *H.* *Lead spacing washer.*

FIG. 2.
Drying of pyridine.

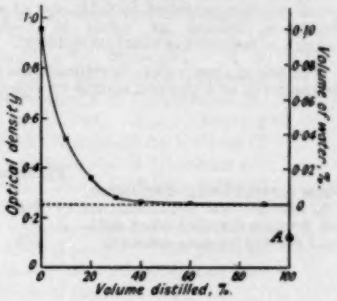
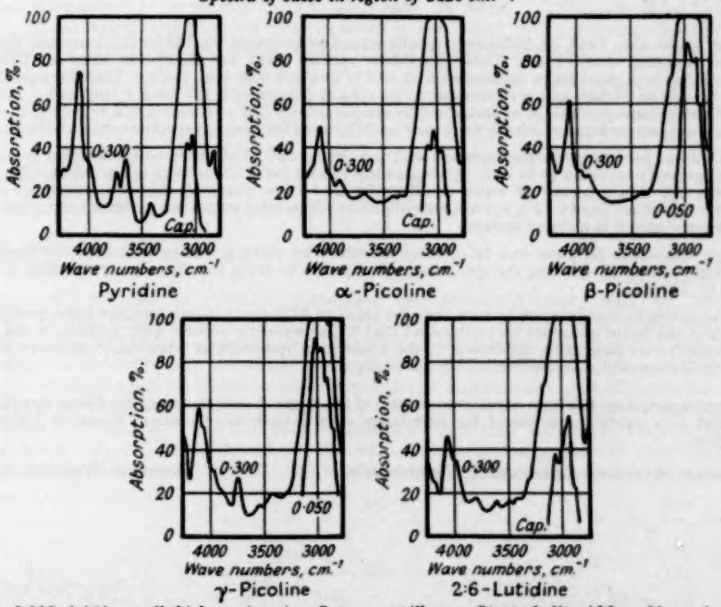


FIG. 3.
Spectra of bases in region of 3420 *cm.*$^{-1}$.



0·300, 0·050 = *cell thickness (mm.).* *Cap.* = *capillary.* *Spectral slit width* = 20 *cm.*$^{-1}$.

The optical density (1-mm. cell) at 3420 cm.$^{-1}$ is plotted in Fig. 2 against the volume percentage of pyridine distilled. As expected from a consideration of the relative boiling points of the azeotrope and pyridine, and of the Rayleigh distillation equation, the optical-density curve approaches an asymptotic

value quite rapidly. Clearly, completely dry pyridine has some absorption near 3420 cm.$^{-1}$ and as can be seen from Fig. 3 this base itself exhibits a weak band at this wave-length.

The higher-boiling bases are more easily dried by the distillation technique than is pyridine, as can be seen from Table I; the spectra of the dry bases in the region 3000—4000 cm.$^{-1}$ are given in Fig. 3. All the bases show some absorption in this region but only pyridine has a well-marked absorption band.

By the addition of known amounts of water it was shown that the optical density varied linearly with the volume percentage of water for each base up to a water concentration of at least 0·2% v/v. A 0·300-mm. absorption cell was found to be convenient for the estimation of water in the range 0·005—0·20% *v/v*. Table II summarises the results for (*a*) optical density of the dry base, and (*b*) the change in optical density produced by 0·1% v/v of water, each expressed in terms of a 1-mm. cell. The optical density is defined as equal to [−log (percentage transmission/100)] or alternatively as [−log{1 − (percentage absorption/100)}].

The use of these values to estimate the water content of a base sample may be illustrated by data on the spectrum of a purified sample of α-picoline (purity 99·8 mol. %) published by Freiser and Glowacki

TABLE I.

	Pyridine.	α-Picoline.	β-Picoline.	γ-Picoline.	2 : 6-Lutidine.
Water content before distillation, % v/v	0·1	0·3	3·0	0·3	1·5
Vol. fraction distilled when optical density became constant	0·9	0·5	0·5	0·3	0·3

TABLE II.

	Pyridine.	α-Picoline.	β-Picoline.	γ-Picoline.	2 : 6-Lutidine.
Optical density of dry base in 1-mm. cell	0·253	0·293	0·285	0·329	0·275
Change in optical density produced by 0·1% v/v of water	0·700	0·664	0·612	0·670	0·671

(*J. Amer. Chem. Soc.*, 1948, **70**, 2575) and recently issued as spectrum No. 743 by the American Petroleum Institute Research Project 44. These published spectra show an absorption band at 3420 cm.$^{-1}$ corresponding to a percentage transmission of 86·5% in a cell 0·08 mm. thick. This corresponds to an optical density of 0·0630, and is equivalent to an optical density of 0·787 for a 1 mm. cell. Thus from Table II the volume percentage of water in this sample is 0·1(0·787 − 0·293)/0·664 = 0·07% v/v. This estimate is only approximate because there may be differences between the spectrometers and in technique.

This volume percentage corresponds to a mol. percentage of 0·41 of water, which is rather greater than the total impurity reported (0·24 mol. %), but unless special precautions were taken during filling of the absorption cell this quantity of water could easily have been absorbed during transference—indeed concentrations of less than 0·02% v/v are very difficult to determine unless the pyridine can be transferred to the absorption cell in a closed system.

Larger quantities of water can be determined either by using a thinner cell with the appropriate calibration curve or by diluting the specimen with dry base to bring the water content within the range covered by Table II.

In conclusion it is of interest to note that the band at 3420 cm.$^{-1}$ is only present when pyridine and water are in the liquid phase for we have found that 3% of water by volume with pyridine in the vapour phase produces no detectable difference in the absorption spectrum at 3420 cm.$^{-1}$ although pyridine vapour itself shows little absorption at this wave-length.

The work described has been carried out as part of the research programme of the Chemistry Research Board and this paper is published by permission of the Director, Chemical Research Laboratory, Teddington.

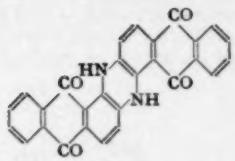
CHEMICAL RESEARCH LABORATORY, TEDDINGTON. [*Received, April 16th*, 1951.]

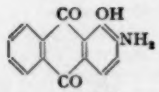
470. *Chemistry of Indanthrone. Part I. The Mode of Formation of Indanthrone from 2-Aminoanthraquinone and Potassium Hydroxide.*

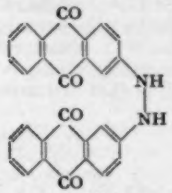
By William Bradley and Edward Leete.

Since 1901, when Bohn discovered indanthrone (I), several theories have been advanced to account for its formation by alkali fusion of 2-aminoanthraquinone. It has been generally held that the reaction of 2-aminoanthraquinone and intermediates derived from it depends on their ability to assume quinonoid forms. This view is shown to be untenable. It is considered that 2-aminoanthraquinone yields the 2-anthraquinonylamine anion, which then replaces hydrogen in another molecule of 2-aminoanthraquinone forming 2-amino-1 : 2′-dianthraquinonylamine (VI). The cyclisation of (VI) to (I) occurs with great ease. Similarly, the *N*-methyl derivatives of (VI) readily yield the corresponding *N*-methyl derivatives of (I); these are also prepared directly from (I) by methylation. The alkali-salt forming properties of 2-aminoanthraquinone and its derivatives are described, as well as experiments on the replacement of nuclear hydrogen in 2-aminoanthraquinone and its *N*-derivatives by hydroxyl and anilino-groups. The physical and chemical properties of numerous derivatives of anthraquinone are recorded, including those of the methyl derivatives of indanthrone.

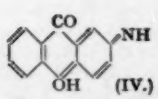
History.—In 1901, an attempt to extend the Heumann synthesis of indigo led Bohn to the discovery of indanthrone (G.P. 129,845). He obtained it, together with alizarin, flavanthrone, and other products, by heating 2-aminoanthraquinone with potassium hydroxide. Bohn ascertained the composition of the new colouring matter and assigned to it the structure (I) which was later found to be correct (Scholl, *Ber.*, 1903, **36**, 3410). Bohn considered that, just as 2-hydroxyanthraquinone afforded alizarin when it was fused with potassium hydroxide, so 2-aminoanthraquinone should yield 2-amino-1-hydroxyanthraquinone (II), and finally

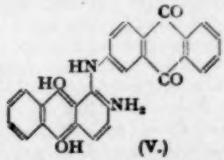

(I.)

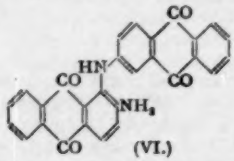

(II.)


(III.)

indanthrone by dehydration. Scholl, Berblinger, and Mansfield (*ibid.*, 1907, **40**, 320) were unable to confirm Bohn's views of the mechanism of the reaction, and Scholl and Eberl (*Monatsh.*, 1911, **32**, 1035) showed further that 2-hydroxylaminoanthraquinone was not an intermediate in the formation of indanthrone. Scholl and Eberl (*loc. cit.*) believed that *s*-di-2-anthraquinonylhydrazine (III) might be a precursor of indanthrone, but Kopetschni (*Chem. Zentr.*, 1924, II, 2506) showed that indanthrone was formed from (III) only by the agency of strong acids. Scholl and Eberl (*loc. cit.*) suggested further that the enolic form of 2-aminoanthraquinone (IV), if formed, should combine with 2-aminoanthraquinone to yield the adduct (V), from which indanthrone itself should result by repetition of the processes of enolisation

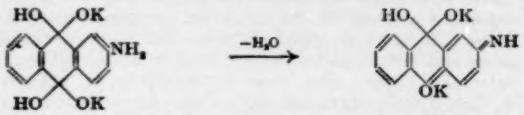

(IV.)


(V.)

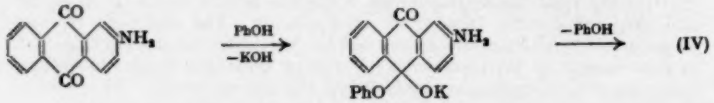

(VI.)

addition, and finally oxidation. The imine-addition hypothesis was adopted by Barnett ("Anthracene and Anthraquinone," London, 1921, p. 344), who regarded 2-amino-1 : 2′-di-

anthraquinonylamine (VI) as the most probable intermediate in the formation of indanthrone. Maki (*J. Soc. Chem. Ind. Japan, Suppl.*, **1929**, **32**, 303) adopted the same hypothesis. He observed that 2-aminoanthraquinone, when added to molten potassium hydroxide, yielded a violet melt from which 2-aminoanthraquinone could be regenerated unchanged by addition of water; this was interpreted as an addition of potassium hydroxide followed by loss of water, the changes being reversible :

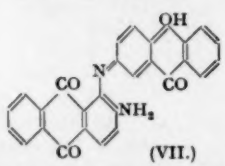


Maki further observed (*ibid.*, **1934**, **37**, 748) that the yield of indanthrone was increased by adding phenol to the melt; this was ascribed to a catalytic action of phenol :

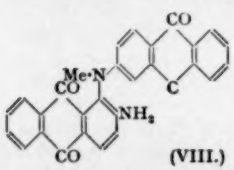


Tanaka (*J. Chem. Soc. Japan*, 1935, **56**, 192) also held that indanthrone formation depended on the occurrence of imine salts. Two other points of view have been advanced by Schwenk (*Chem.-Ztg.*, 1928, **52**, 45) who favoured a quinonoid-ion-radical hypothesis, and by Bradley and Robinson (*J.*, 1932, 1254), who considered the formation of indanthrone to be an instance of aromatic substitution, the anion of 2-aminoanthraquinone replacing nuclear hydrogen in a second molecule of the amine.

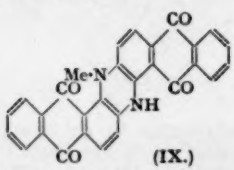
The Imine-addition Hypothesis.—In the present experiments 2-amino-1 : 2′-dianthraquinonylamine (VI) has been prepared and shown to yield indanthrone (I) under a wide variety of conditions involving the use of acid, neutral, and alkaline media. There can be no doubt that if (VI) is produced as a result of the action of alkalis on 2-aminoanthraquinone, then its cyclisation to indanthrone will follow. Experiments in support of this conclusion are described in Part III. Whether the cyclisation of (VI) to indanthrone requires enolisation of (VI) as an essential step, giving (VII) at an intermediate stage, has been answered by experiments with the *N*-methyl derivative (VIII), which is incapable of affording an analogous enolic form.



(VII.)

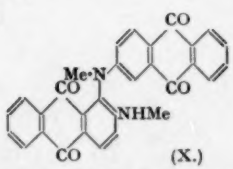


(VIII.)

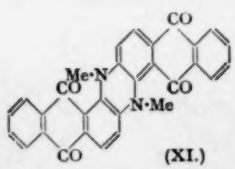


(IX.)

Heating (VIII) with a suspension of potassium hydroxide in pyridine sufficed to convert it into *N*-methylindanthrone (IX), identical with the monomethyl derivative prepared by the direct methylation of indanthrone. In other experiments the dimethyl derivative (X) was prepared and shown to be easily cyclised to *NN*-dimethylindanthrone (XI) identical with the dimethyl derivative prepared from indanthrone directly or by methylating the monomethyl derivative (IX).



(X.)

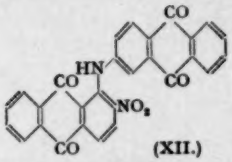


(XI.)

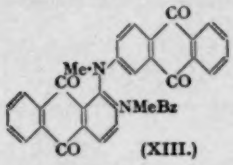
These results indicate that enolisation of the anthraquinone nucleus is not an essential step in the process leading to the linking of the nitrogen of amino- or methylamino-groups with the

nucleus. Further, if, as would be expected, the same considerations apply to the union of two molecules of 2-aminoanthraquinone to give (VI), it must be concluded that enolisation of 2-aminoanthraquinone forming (IV) is not an essential initial step in the process.

The 2-amino-1 : 2′-dianthraquinonylamine employed in these experiments was prepared by condensing 1-chloro-2-nitroanthraquinone with 2-aminoanthraquinone to form (XII), and reducing the product. 1-Chloro-2-nitroanthraquinone is highly reactive; heating it for only a few moments with diethylamine yields 1-diethylamino-2-nitroanthraquinone. Similarly, attempts to improve the preparation of (XII) by addition of potassium acetate led to 1-hydroxy-2-nitroanthraquinone as the main product, the 2-aminoanthraquinone present as a reactant being recovered unchanged.



(XII.)



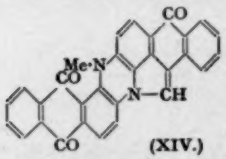
(XIII.)

1-Chloro-2-nitroanthraquinone was first prepared by Kopetschni (G.P. 363,930) by oxidising 2-amino-1-chloroanthraquinone with persulphuric acid. We used Kopetschni's method with success, but the preparation was inconvenient because of the simultaneous formation of by-products. Better results were obtained by applying Hodgson, Mahadevan, and Ward's method (*J.*, 1947, 1392) for the replacement of amino- by nitro-groups to 2-amino-1-chloroanthraquinone.

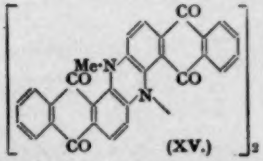
Methylation of 2-nitro-1 : 2′-dianthraquinonylamine gave the *N*-methyl derivative, and this, on reduction, gave 2-amino-1 : 2′-dianthraquinonyl-*N*-methylamine (VIII). The *N*-benzoyl derivative of (VIII) was methylated to give (XIII), and subsequent hydrolysis afforded (X).

2-Nitro-1 : 2′-dianthraquinonylamine formed a deep red addition complex with 0·5 mol. of chlorobenzene. It also combined with toluene, but not with benzene. The addition compounds had considerable stability towards heat; they were readily dissociated by mixing them with ether or ethyl acetate.

Methylation of Indanthrone.—Indanthrone was converted into a mixture of *N*-mono- and *NN*-di-methylindanthrone by heating it in trichlorobenzene with methyl toluene-*p*-sulphonate and dry potassium carbonate. The methyl derivatives were more soluble than indanthrone which remained undissolved in the form of a green alkali derivative. The character of the insoluble product was shown by adding a drop of acetic acid to its suspension in *o*-dichlorobenzene, the liberated indanthrone dispersing in the medium with a blue colour. Water also hydrolysed the green alkali derivative, yielding indanthrone. The trichlorobenzene solution containing the methyl derivatives gave coppery-blue needles of *NN*-dimethylindanthrone (XI); the mother-liquor was chromatographed on alumina; the two main zones were blue, the upper one consisting of (XI), and the lower zone containing a colouring matter (B) which resembled *N*-methylindanthrone (IX) in composition.



(XIV.)



(XV.)

Product B resembled indanthrone and its *N*-methyl and *NN′*-dimethyl derivatives in colour, absorption spectrum in sulphuric acid (see Fig. 1), and in the absorption spectrum in alkaline solution of the brown reduction product obtained by heating it with alkaline dithionite (hydrosulphite) (see Fig. 2). All four colouring matters behaved similarly on quantitative hydrogenation, but B differed from indanthrone and *N*-methylindanthrone in showing no reaction with nitric acid in sulphuric acid, or with potassium hydroxide in pyridine. B differed markedly from *NN′*-dimethylindanthrone in the character of its absorption in pyridine (Fig. 3). It could not be prepared by heating dimethylindanthrone with potassium carbonate in trichlorobenzene. The properties of B are those expected of (XIV), but the mode of derivation of such a compound in the methylation of indanthrone is obscure. The hydrazine structure (XV), which

would result from monomethylindanthrone by dehydrogenation, is excluded since B cannot be converted into indanthrone by demethylation.

Alkali-salt Formation in Derivatives of 2-Aminoanthraquinone.—It has been shown by one of us (*J. Soc. Dyers Col.*, 1942, **58**, 2) that the occurrence of acid characters in derivatives of anthraquinone and many related compounds can be readily demonstrated by adding a drop of a concentrated methanolic potassium hydroxide to a solution of the derivative in dry pyridine. In most instances a marked change is observed in the colour of the solution, and the change is reversed on addition of water or alcohol immediately when the derivative is a very weak acid, less readily when it is stronger. In the present experiments the colour change was dependent on the occurrence of NH⁻ groups attached to an aromatic nucleus and generally, but not invariably, situated either *ortho* or *para* to a carbonyl group.

The pyridine–alkali colour test provided a most useful guide to the progress of reactions involving the conversion of secondary amines into amides and tertiary amines, and to the

FIG. 1. FIG. 2. FIG. 3.

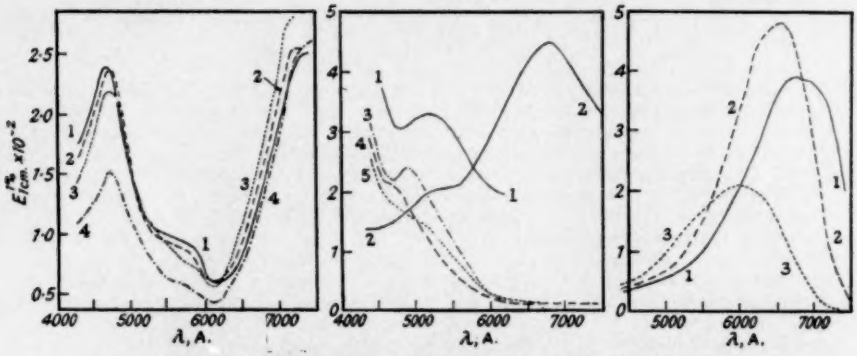


FIG. 1.—*Indanthrone and its* N-*methyl derivatives in concentrated sulphuric acid.*

1, *Indanthrone : Max. at* 4650 Å. (E = 240), *min. at* 6150 Å. (E = 61).
2, N-*Methylindanthrone : Max. at* 4700 Å. (E = 235), *min. at* 6100 Å. (E = 62).
3, NN-*Dimethylindanthrone : Max. at* 4720 Å. (E = 217), *min. at* 6100 Å. (E = 57).
4, *Product B : Max. at* 4750 Å. (E = 150), *min. at* 6100 Å. (E = 44).

FIG. 2.—*Solutions obtained by dissolving indanthrone and its* N-*methyl derivatives in sodium hydroxide containing sodium dithionite.*

1, *Indanthrone, brown solution (tetrahydro-derivative) : Min. at* 4800 Å. (E = 305), *max. at* 5150 Å. (E = 330).
2, *Indanthrone, blue solution (dihydro-derivative) : Max. at* 6800 Å. (E = 450).
3, N-*Methylindanthrone, brown solution : Min. at* 4700 Å. (E = 220), *max. at* 4900 Å. (E = 240).
4, NN-*Dimethylindanthrone.*
5, *Product B.*

FIG. 3.—N-*Methyl derivatives of indanthrone in pyridine.*

1, N-*Methylindanthrone : Max. at* 6700 Å. (E = 390).
2, NN-*Dimethylindanthrone : Max. at* 6550 Å. (E = 480).
3, *Product B : Max. at* 6000 Å. (E = 210).

homogeneity of amines and amides likely to contain analogous –NH– compounds as impurities.

The formation of metallic derivatives of amines and amides has often been described. Fones (*J. Org. Chem.*, 1949, **14**, 1099) prepared the sodium salt of *p*-methoxyacetanilide by means of sodium hydride; Thielepape (*Ber.*, 1935, **68**, 751) obtained the sodium salt of acetanilide by using the free metal. In one instance, *o*-nitroacetanilide, an alkali derivative results when the amide is dissolved in aqueous sodium hydroxide.

There can be little doubt that the colours produced from anthraquinone derivatives by potassium hydroxide in pyridine are due to alkali salts. Their appearance requires the presence of a free –NH– group in the derivative, the use of a strong base, and the almost complete absence of water or hydroxylic solvents from the medium. Potassium hydroxide was more effective than sodium hydroxide; lithium hydroxide showed little tendency to react. One of the

strongest acids encountered was 2-benzamido-1-nitroanthraquinone. Like *o*-nitroacetanilide it dissolved in aqueous sodium hydroxide; it was precipitated unchanged by addition of acid to the red solution. 2-Acetamido-1-nitroanthraquinone behaved similarly. Both acyl derivatives were readily methylated in alkaline solution with formation of the *N*-benzoyl and *N*-acetyl derivatives of 2-methylamino-1-nitroanthraquinone. The colour of the alkali derivatives depends on the medium: it is bluest in pyridine, morpholine, or acetone, less blue in alcohol, and red in water. It does not appear that the basic solvents have any essential part in the formation of the alkali salts, as similar colours are given in acetone (see Fig. 4).

2-Aminoanthraquinone does not form an alkali salt in pyridine, the colour change to green previously reported (*J. Soc. Dyers and Col.*, 1942, **58**, 2) being due to the presence of very small

FIG. 4. FIG. 5. FIG. 6.

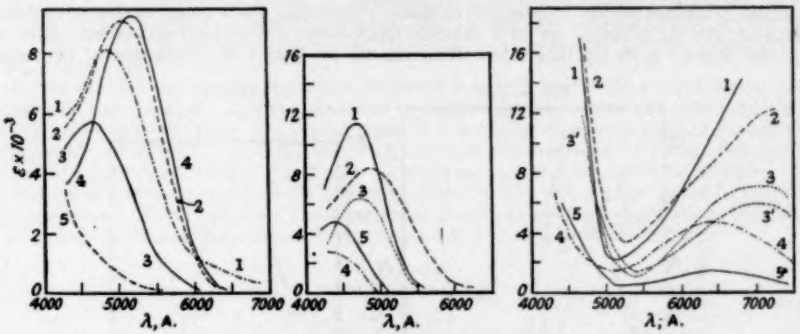


FIG. 4.—*The potassium salt of 2-benzamido-1-nitroanthraquinone in various solvents.*

1, *Morpholine: Max. at* 4850 Å. (ε = 8150).
2, *Acetone: Max. at* 5050 Å. (ε = 9100).
3, *Ethyl alcohol: Max. at* 4700 Å. (ε = 5700).
4, *Pyridine: Max. at* 5200 Å. (ε = 9200).
5, *Water: no max. or min. observed.*

FIG. 5.—*Derivatives of 2-aminoanthraquinone in pyridine.*

1, 2 : 2′-*Dianthraquinonylamine: Max. at* 4700 Å. (ε = 11,400).
2, 1 : 2′-*Dianthraquinonylamine: Max. at* 4850 Å. (ε = 8400).
3, 2-*Anilinoanthraquinone: Max. at* 4750 Å. (ε = 6400).
4, 2-*Amino-1-nitroanthraquinones.*
5, 2-*Amino-1-chloroanthraquinone: Max. at* 4400 Å. (ε = 4800).

FIG. 6.—*Solutions in pyridine containing excess of methanolic potassium hydroxide.*

1, 2 : 2′-*Dianthraquinonylamine: Min. at* 5100 Å. (ε = 2300).
2, 1 : 2′-*Dianthraquinonylamine: Min. at* 5250 Å. (ε = 3400).
3, 2-*Anilinoanthraquinone: Min. at* 5400 Å. (ε = 1100), *max. at* 7100 Å. (ε = 7200).
3′, 2-*Anilinoanthraquinone* (*with* NaOH *in place of* KOH): *Min. at* 5400 Å. (ε = 1300), *max. at* 7100 Å. (ε = 6000).
4, 2-*Amino*-1-*nitroanthraquinone: Min. at* 5150 Å. (ε = 1600), *max. at* 6500 Å. (ε = 4700).
5, 2-*Amino*-1-*chloroanthraquinone: Min. at* 5300 Å. (ε = 600), *max. at* 6500 Å. (ε = 1500).

amounts of 2 : 2′-dianthraquinonylamine. 2-Amino-1-nitro-, 2-amino-1-chloro-, and 2-anilinoanthraquinone, and 2 : 2′-, 1 : 2′-, and 1 : 1′-dianthraquinonylamine afford green colours (Figs. 5 and 6). 2-Methylamino-1-nitroanthraquinone gives a pale green colour which is much less intense than that characteristic of the unmethylated nitro-amine. Indanthrone and *N*-methylindanthrone give green colours, *NN*-dimethylindanthrone is unaffected. Acyl derivatives of 2-aminoanthraquinone afford red-violet colours; in all the instances examined, 2-acetamido-, 2-benzamido-, 2-*p*-nitrobenzamido-, and 2-toluene-*p*-sulphonamido-anthraquinone, the wavelength of maximum absorption was in the region 5000—5400 Å. This is also true of 2-benzamidofluorenone. The intensity of the absorption varies with the acyl group; it is highest with the benzoyl and *p*-nitrobenzoyl and less with the acetyl and toluene-*p*-sulphonyl derivatives; the lowest intensity is found in the fluorenone derivatives (Figs. 7 and 8). The presence of carbonyl groups is not essential for the occurrence of acid characters; 2-acetamidoanthracene affords

a colourless solution in pyridine, which becomes yellow on addition of methanolic potassium hydroxide. It is interesting that, unlike 2-anilinoanthraquinone, 1-anilinoanthraquinone exhibits no alkali colour reaction.

Crystalline potassium salts of 2-toluene-*p*-sulphonamidoanthraquinone and its 1-chloro-derivative were readily prepared. Those of 2-benzamido- and 2-*p*-nitrobenzamido-anthraquinone were obtained as amorphous red powders; that of 2-acetamidoanthraquinone prepared in pyridine decomposed when benzene was added. The green sodium salt of 2-anilinoanthraquinone was prepared by the use of sodioanthracene (Schlenk, Appenrodt, Michael, and Thal, *Ber.*, 1914, **47**, 473); it was too unstable for isolation or methylation. The green potassium salt of 1 : 2'-dianthraquinonylamine was easily prepared, but it decomposed rapidly on exposure to air, re-forming the free amine.

2-Aminoanthraquinone as a Substituting Agent.—There is no lack of evidence for the ability of amines to replace nuclear hydrogen in aromatic compounds, when nitro-, carbonyl, or similar groups are already present. In each example replacement of hydrogen occurs only when the reactants include a strong base which functions by promoting the ionisation of the amine.

FIG. 7.

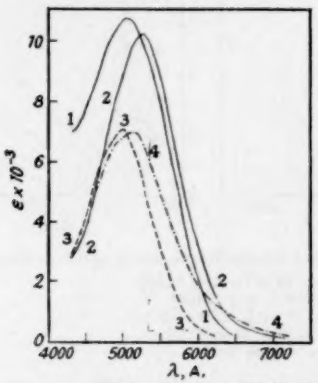


FIG. 8.

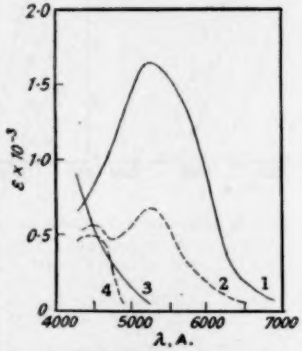


FIG. 7.—*Acylaminoanthraquinones. Solutions in pyridine to which methanolic potassium hydroxide has been added.*

1, 2-p-*Nitrobenzamidoanthraquinone: Max. at* 5060 Å. (ε = 10,800).
2, 2-*Benzamidoanthraquinone: Max. at* 5270 Å. (ε = 10,200).
3, 2-*Toluene*-p-*sulphonamidoanthraquinone: Max. at* 5000 Å. (ε = 7000).
4, 2-*Acetamidoanthraquinone: Max. at* 5150 Å. (ε = 6900).

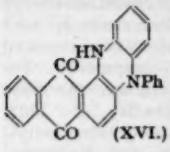
FIG. 8.—*Acylaminofluorenones.*

1, 2-*Benzamidofluorenone in pyridine + methanolic potassium hydroxide: Max. at* 5250 Å. (ε = 1650).
2, 2-*Acetamidofluorenone in pyridine + methanolic potassium hydroxide: Max. at* 5250 Å. (ε = 670).
3, 2-*Benzamidofluorenone in pyridine.*
4, 2-*Acetamidofluorenone in pyridine.*

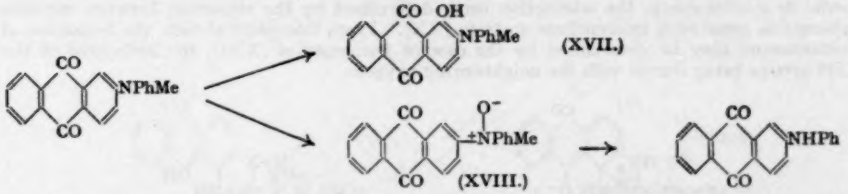
Whilst carbazole has no action on nitrobenzene, its potassium derivative forms *N*-*p*-nitrophenylcarbazole (G. and M. de Montmollin, *Helv. Chim. Acta*, 1923, **6**, 94); ammonia is without action on *meso*benzanthrone, whilst sodamide forms the 6-amino-derivative (Bradley, *J.*, 1948, 1175). Recently it has been stated (F.I.A.T. Final Report, No. 1313, Vol. III, p. 82) that 2-aminoanthraquinone heated with "caustic" in nitrobenzene yields 2-*p*-nitroanilinoanthraquinone. We have confirmed this result when using potassium hydroxide as condensing agent, and proved the constitution of the product by preparing it from 2-chloroanthraquinone and *p*-nitroaniline. It was not possible to condense 2-aminoanthraquinone with *meso*benzanthrone, but the dimethylaniline used as solvent may have contributed to this by reducing the concentration of the reactants. The successful condensation of 2-aminoanthraquinone with nitrobenzene, however, provides a clear instance of the ability of 2-aminoanthraquinone to function as a substituting agent. In effectiveness it does not approach sodamide or sodamide–piperidine (Bradley, *J.*, 1948, 1175), but it has the same order of activity as the potassium derivative of carbazole. In order to observe the effect of increasing the acid strength of 2-aminoanthraquinone we attempted

the condensation of 2-amino-1-nitroanthraquinone with nitrobenzene, but without success; this illustrates the rule that only the anions of the weakest acids are able to replace nuclear hydrogen in aromatic nitro- or carbonyl compounds.

Substitution in 2-Aminoanthraquinone and its N-Derivatives.—Tanaka (*J. Chem. Soc. Japan*, 1935, **56**, 192) and Maki (*loc. cit.*) have shown that when 2-aminoanthraquinone is heated with potassium hydroxide in the presence of an oxidant 2-amino-1-hydroxyanthraquinone is formed; under appropriate conditions the yield is 50%. G.P. 360,530 describes the formation of 2-amino-1-anilinoanthraquinone by the action of sodamide–aniline on 2-aminoanthraquinone; 2-anilinoanthraquinone is stated to yield 1 : 2-dianilinoanthraquinone. In G.P. 329,246 it is claimed that 2-anilinoanthraquinone heated with aniline and powdered potassium hydroxide yields 5 : 10-dihydro-5-phenyl-1 : 2-phthaloylphenazine (XVI). These reactions illustrate the ability of 2-aminoanthraquinone and 2-anilinoanthraquinone to undergo substitution at the 1-position by hydroxyl and anilinium ions.

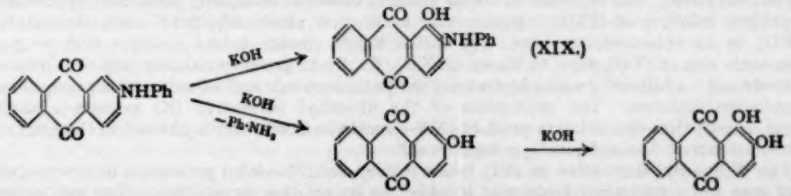

(XVI.)

In the present experiments the alkali fusion of 2-anilino- and 2-*N*-methylanilino-anthraquinone has been studied. Heating the latter with potassium hydroxide and potassium nitrate gave 2-anilinoanthraquinone (3%), unchanged 2-*N*-methylanilinoanthraquinone (more than 50%), and a reddish-brown product, m. p. 200—205°, considered to be 1-hydroxy-2-*N*-methylanilinoanthraquinone (XVII); there was no evidence for the formation of alizarin. The production of 2-anilinoanthraquinone probably occurs by way of the amine oxide (XVIII) and subsequent loss of formaldehyde. The formation of (XVII) may involve the direct hydroxylation of 2-*N*-methylanilinoanthraquinone or rearrangement of the amine oxide (XVIII).


(XVII.) (XVIII.)

Fusion of 2-anilinoanthraquinone with potassium hydroxide gave alizarin, aniline, and a potassium salt. The last is derived from a violet substance, m. p. 225—226°, which is considered to be 2-anilino-1-hydroxyanthraquinone (XIX) as it gives a boroacetate reaction (Dimroth, *Annalen*, 1926, **446**, 97) and the potassium salt is stable towards fused potassium hydroxide.

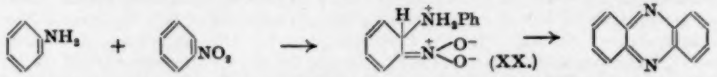
Alkali fusion of 2-anilinoanthraquinone at a higher temperature increased the yield of alizarin, but diminished that of the 2-anilino-1-hydroxyanthraquinone. It appears, therefore, that alizarin results by the hydroxylation of 2-hydroxyanthraquinone, itself produced by hydrolysis of 2-anilinoanthraquinone:


(XIX.)

In this example, the formation of (XIX) cannot be ascribed to the intermediate formation of an amine oxide, but hydroxylation of an imino-form of 2-anilinoanthraquinone cannot be excluded. If, however, as is probable, hydroxylation of 2-anilino- and 2-*N*-methylanilino-anthraquinone occurs by the same mechanism, the process in both cases must be the direct replacement of nuclear hydrogen by hydroxyl, as occurs in *meso*benzanthrone (Bradley and Jadhav, *J.*, 1937, 1791).

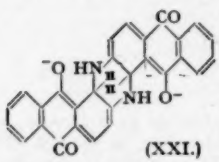
Neither 2-anilinoanthraquinone nor its *N*-methyl derivative yields a derivative of indanthrone on fusion with potassium hydroxide.

The replacement of a hydrogen atom situated *ortho* to a carbonyl group by an amino- or substituted amino-group is a normal reaction, but the problem remains why replacement of hydrogen occurs exclusively at the 1-position in 2-aminoanthraquinone. We consider that the result is determined by the unusual stability of indanthrone, and that, although there are several theoretically possible ways in which 2-aminoanthraquinone may replace a hydrogen atom in a second molecule of the same, the stability factor operates to favour the orientation which leads to indanthrone. Ultimately, the result must be determined by the high resonance energy of the product or some intermediate which precedes it. This high resonance energy may explain many of the unexpected variations in the orientation of substituents which have replaced nuclear hydrogen in aromatic ketones, nitro-compounds, and analogous compounds. For example, whilst sodamide and *meso*benzanthrone yield 6-amino*meso*benzanthrone, the same ketone with sodamide–piperidine yields 4-piperidino*meso*benzanthrone (Bradley, *J.*, 1937, 1091). Nitrobenzene with the potassium derivative of carbazole affords *p*-nitrophenylcarbazole; sodamide–piperidine affords *p*-nitrophenylpiperidine (Bradley and Robinson, *loc. cit.*). On the other hand, potassium hydroxide reacts with nitrobenzene to give mainly *o*-nitrophenol (Wohl, *Ber.*, 1899, **32**, 2486; Wohl and Aue, *ibid.*, 1901, **34**, 2444). It is probable that the condensation of aniline and potassium hydroxide with nitrobenzene to form phenazine,

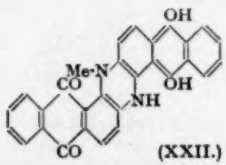


(XX.)

and of 2-naphthylamine with nitrobenzene to form 1 : 2-benzophenazine (Wohl, *Ber.*, 1903, **36**, 4135), are both normal examples of the replacement by amines of nuclear hydrogen situated *ortho* to a nitro-group, the orientation being determined by the attraction between opposite charges in some such intermediate state as (XX). From this point of view the formation of indanthrone may be determined by the ease of formation of (XXI), the hydrogens of the NH groups being shared with the neighbouring oxygens.



(XXI.)



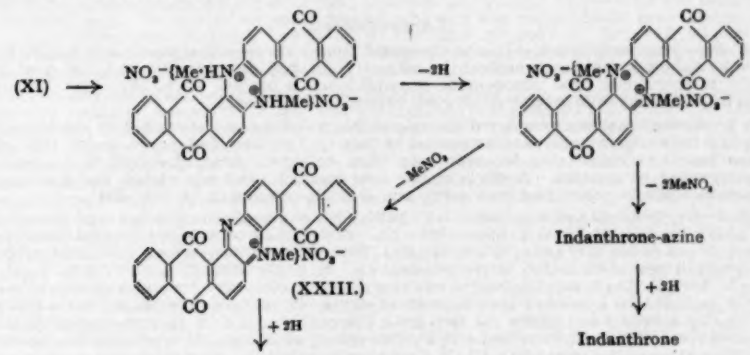
(XXII.)

The methyl derivatives of 2-amino-1 : 2′-dianthraquinonylamine (VI) differed from the parent amine in regard to the conditions in which cyclisation to an indanthrone occurred. Whilst (VI) yielded indanthrone when merely heated alone or suspended in neutral media, or even in boiling acetic acid, as well as by the action of potassium hydroxide in its solution in pyridine, with the methyl derivatives the use of alkaline media was necessary for ring-closure. Both potassium hydroxide and sodium hydroxide were used successfully; lithium hydroxide was not effective. The sequence of colour changes observed on adding potassium hydroxide to a pyridine solution of (VIII) suggests that cyclisation yields dihydro-*N*-methylindanthrone (XXII) at an intermediate stage The initial bright orange colour changes first to green [potassium salt of (VI)], then to brown (XXII), finally to green (potassium salt of *N*-methylindanthrone); addition of water hydrolyses the potassium salt and affords a blue precipitate of *N*-methylindanthrone. The cyclisation of the dimethyl derivative (X) pursues a similar course, except that the ultimate product (*NN*-dimethylindanthrone) is present in the form of a blue solution as it does not yield a potassium salt.

The *N*-benzoyl derivative of (VI) forms a deep reddish-violet potassium derivative with great ease when potassium hydroxide is added to its solution in pyridine. The salt is quite stable to heat in the medium in which it is prepared, but shows no tendency to cyclise to an indanthrone derivative. This provides a further illustration of the rule that an increase in the acid properties of an amine may diminish its effectiveness as a substituting agent for a nucleus with predominantly cationoid reactivity.

Properties of Indanthrone and its N-*Methyl Derivatives.*—Indanthrone and its *N*-methyl and *NN*-dimethyl derivatives are blue dyes which dissolve in concentrated sulphuric acid forming brown solutions. The solubility in organic solvents increases progressively with the degree of methylation, which suggests the occurrence of intermolecular bonding (−NH . . . OC−) in

indanthrone and to a smaller degree in its monomethyl derivative. A similar relation is found between the three isomeric dianthraquinonylamines (less soluble) and their methyl ethers (more soluble). Further, 2 : 2′-dianthraquinonylamine does not sublime, whilst its *N*-methyl ether does so readily. Intermolecular bonding appears to be less prominent in 1 : 1′-dianthraquinonylamine, which not only sublimes readily, but is also more soluble in organic solvents than the 2 : 2′-isomer. Both indanthrone and its *N*-methyl derivative form alkali salts with potassium hydroxide in pyridine; the *NN*-dimethyl derivative does not. The two methyl ethers dissolve in alkaline dithionite forming brown solutions; indanthrone forms two reduction products which yield, respectively, a blue and a brown solution. The behaviour of the three colouring matters on oxidation is characteristic. Nitric acid alone, or in solution in concentrated sulphuric acid, rapidly dehydrogenates indanthrone to indanthrone-azine (Scholl and Berblinger, *Ber.*, 1903, **36**, 3427). *N*-Methylindanthrone is similarly oxidised; a quaternary nitrate (XXIII) separates from the solution in the form of orange crystals. *NN*-Dimethylindanthrone is much more stable: it is not affected by nitric acid in sulphuric acid, but concentrated nitric acid causes demethylation and formation of (XXIII). Reduction of this product by alkaline dithionite, and subsequent aeration of the solution, yield *N*-methylindanthrone. A small quantity of indanthrone-azine is formed also by the action of nitric acid on *NN*-dimethylindanthrone, being recognized by reduction of the oxidation product and chromatography of the reduced form on cellulose; the reduced form of indanthrone has a higher affinity for cellulose than either of its methyl derivatives. The course of the oxidation of *NN*-dimethylindanthrone may be represented by the scheme:



Sodium hypochlorite containing 10% of available chlorine oxidises indanthrone to a green derivative but is without action on *NN*-dimethylindanthrone.

A number of analogous demethylations have been observed in the phenazine series. McIlwain (*J.*, 1937, 1704) found that *N*-methylphenazinium hydroxide decomposed in aqueous solution yielding phenazine, and Clemo and McIlwain (*J.*, 1935, 738) have shown that *NN*-dimethyldihydrophenazine yields phenazine, when its solution is exposed to air. Similarly, oxidation of pyocyanine yields formic acid and 1-hydroxyphenazine (Wrede and Strack, *Ber.*, 1929, **62**, 2054).

The preparation of several intermediates of general interest was investigated during the work. 2-Nitroanthraquinone was best prepared from 2-aminoanthraquinone by the diazonium reaction; on fusion with potassium hydroxide it yielded alizarin. 2-Anilinoanthraquinone was obtained by prolonged heating of aniline with 2-chloroanthraquinone. The use of 2-iodoanthraquinone did not afford a better yield; the method of G.P. 288,464, involving the heating of anthraquinone-2-sulphonic acid with aniline and potassium hydroxide in a current of air, was less satisfactory than the method finally employed. In an attempt to hasten the reaction between 2-chloroanthraquinone and aniline, a solution of sodium anilide in aniline was used. The main product was a blue compound, m. p. 236—237°, having the same composition as a product, m. p. 233°, obtained, according to G.P. 329,246, when 2-anilinoanthraquinone was heated with aniline and powdered potassium hydroxide. The structure assigned to the product of m. p. 233° is 5 : 10-dihydro-5-phenyl-1 : 2-phthaloylphenazine (XVI). The compound of

m. p. 236—237° dissolves in pyridine with a blue colour, unchanged by addition of methanolic potassium hydroxide; in this it resembles 1-anilinoanthraquinone but differs from 2-anilinoanthraquinone. It is probably correctly represented by (XVI).

2 : 2′-Dianthraquinonylamine was obtained only in poor yield by existing methods (Eckert and Steiner, *Monatsh.*, 1914, **35**, 1133; G.P. 162,824) Ultimately it was prepared satisfactorily from 2-aminoanthracene, by way of di-2-anthrylamine (Bollert, *Ber.*, 1883, **16**, 1635), forming its *N*-benzoyl derivative, and *NN*-di-2-anthraquinonylbenzamide.

In an attempt to prepare 2-anilino-1-hydroxyanthraquinone, 2-chloro-1-nitroanthraquinone was heated with aniline; the product was 1-anilino-2-chloroanthraquinone. According to Schmidt (*Bull. Soc. Ind. Mulhouse*, 1914, **84**, 409) an analogous replacement of an α-nitro-group occurs when 1-nitroanthraquinone is heated with aniline.

Difficulty was at first encountered in methylating 1 : 2′-dianthraquinonylamine; the successful methyl toluene-*p*-sulphonate–trichlorobenzene–potassium carbonate procedure (p. 2140) was also successful with 2 : 2′-dianthraquinonylamine, indanthrone, *N*-methylindanthrone, 2-nitro-1 : 2′-dianthraquinonylamine, 2-anilino- and 2-benzamido-anthraquinone, and 2-benzamido-1 : 2′-dianthraquinonyl-*N*-methylamine. In some instances the medium employed was *o*-dichlorobenzene. The potassium salt of 2-toluene-*p*-sulphonamidoanthraquinone was readily alkylated to form the methyl, ethyl, and *n*-butyl derivatives, from which were prepared 2-methylamino- and 2-ethylamino-anthraquinone. Similarly 1-chloro-2-toluene-*p*-sulphonamidoanthraquinone afforded the methyl derivative, from which 1-chloro-2-methylaminoanthraquinone was prepared and its *N*-acetyl and *N*-benzoyl derivatives.

Experimental.

1 : 2′-*Dianthraquinonylamine.*—This was prepared from 1-chloroanthraquinone and 2-aminoanthraquinone by Eckert and Steiner's method (*loc. cit.*). It sublimed with difficulty at 1 mm. from a bath at 330°; it crystallised from nitrobenzene in reddish-brown needles, m. p. 387—388°. Its orange solution in acetic anhydride became violet when warmed with boric acid.

The 2-aminoanthraquinone employed throughout this investigation was purified by crystallisation of the sulphate from sulphuric acid as recommended by Maki (*J. Soc. Chem. Ind. Japan, Suppl.*, 1933, **36**, 44). The free base was regenerated by hydrolysis, then collected, dried, dissolved in benzene, and chromatographed on alumina. A single orange zone resulted; this was eluted, and the recovered 2-aminoanthraquinone crystallised from acetic acid as orange needles, m. p. 306—307°.

N-Benzoyl-1 : 2′-*dianthraquinonylamine.*—1 : 2′-Dianthraquinonylamine (0·5 g.) was heated under reflux during 4 hours with benzoyl chloride (25 c.c.). The solution, initially red, became yellow-brown. The solution was cooled, then added to ethyl alcohol (100 c.c.); the *N-benzoyl* derivative slowly separated, and crystallised from acetic acid as yellow prisms (0·4 g.), m. p. 272—273° (Found: N, 2·7. $C_{35}H_{19}O_3N$ requires N, 2·6%). The benzoyl derivative was very readily hydrolysed. Its yellow solution in pyridine remained unaltered for a moment after addition of methanolic potassium hydroxide, but a pale green colour quickly appeared and finally the deep green characteristic of 1 : 2′-dianthraquinonylamine. It dissolved in concentrated sulphuric acid with a yellow colour, which changed to greenish-blue on storage; the addition of water then precipitated 1 : 2′-dianthraquinonylamine. Hydrolysis also occurred readily during the preparation of the benzoyl derivative if the hot solution in benzoyl chloride was added to water.

1 : 2′-*Dianthraquinonyl-N-methylamine.*—1 : 2′-Dianthraquinonylamine (2·1 g.), methyl toluene-*p*-sulphonate (2·5 g.), and dry potassium carbonate (1·0 g.) were heated under reflux in trichlorobenzene (40 c.c.) during 5 hours. The hot solution was filtered, and the residue washed with more of the hot solvent. Filtrate and washings were concentrated to 15 c.c. and then mixed with light petroleum. A red *amine* separated (1·5 g.), which recrystallised from acetic acid as red needles (1·3 g.), m. p. 284—285° (Found: N, 3·1. $C_{29}H_{17}O_4N$ requires N, 3·2%). 1 : 2′-Dianthraquinonyl-*N*-methylamine dissolved in pyridine with an orange colour, unaffected by addition of methanolic potassium hydroxide. It dissolved in sulphuric acid with a pale green colour; when warmed, the solution became reddish-violet. The base was not affected by an hour's boiling with benzoyl chloride containing a small proportion of concentrated sulphuric acid. It was more soluble in organic solvents than was 1 : 1′-dianthraquinonyl-*N*-methylamine.

2 : 2′-*Dianthraquinonylamine.*—(*a*) The following procedure is an improvement on that of Eckert and Steiner (*loc. cit.*). An intimate mixture of 2-aminoanthraquinone (4·4 g.), 2-chloroanthraquinone (4·8 g.), and anhydrous potassium carbonate (2·0 g.) was made into a paste with nitrobenzene (10 c.c.) and heated at 270—290° for 6 hours. The black product was washed by alcohol, the residue (6·5 g.) was dissolved in nitrobenzene (300 c.c.), and the solution treated with charcoal and then filtered. Copper-coloured plates of 2 : 2′-dianthraquinonylamine separated (0·2 g.). These decomposed without melting at about 500° (Found: N, 3·6. Calc. for $C_{28}H_{15}O_4N$: N, 3·3%).

(*b*) 2 : 2′-Dianthrylamine was prepared from 2-aminoanthracene by Bollert's method (*Ber.*, 1883, **16**, 1635). A suspension containing 2 : 2′-dianthrylamine (12·4 g.) and benzoyl chloride (50 c.c.) in pyridine (100 c.c.) was heated under reflux for 2 hours. The resulting pale brownish-yellow solution was added to alcohol (150 c.c.); the *benzoyl* derivative separated in pale yellow needles (13·5 g.), m. p. 248—249° (Found: N, 3·3. $C_{35}H_{22}ON$ requires N, 3·0%). It dissolves in concentrated sulphuric acid with a reddish-brown colour; water changes the colour to yellow.

Powdered chromium trioxide (25 g.) was added in small successive amounts to a solution containing dianthrylbenzamide (13·5 g.) in boiling acetic acid (1 l.). The addition complete, boiling was continued for 10 minutes, and then the solution was added to water (3 l.). The yellow precipitate was collected, washed with water, dried (yield, 13·7 g.), and recrystallised from acetic acid. Small yellow prisms separated, of m. p. 267—268° (Found: C, 78·4; H, 3·7; N, 2·7. $C_{28}H_{15}O_3N$ requires C, 78·8; H, 3·6; N, 2·6%). Yield, 10·2 g. NN-2 : 2′-*Dianthraquinonylbenzamide* affords a pale yellow solution in pyridine; addition of methanolic potassium hydroxide causes hydrolysis almost immediately, a deep green solution being formed.

A solution containing *NN*-2 : 2′-dianthraquinonylbenzamide (8·0 g.) in concentrated sulphuric acid was heated for an hour at 100°; the yellow-orange solution became deep blue. The solution was then cooled and added to water, and the bulky red precipitate collected and washed until neutral. The yield of 2 : 2′-*dianthraquinonylamine* was 6·5 g. A portion recrystallised from 1200 parts of boiling nitrobenzene afforded small, orange-red prisms having a coppery lustre and decomposing about 500° (Found: C, 78·4; H, 3·6; N, 3·3. $C_{28}H_{15}O_4N$ requires C, 78·3; H, 3·5; N, 3·3%). It forms an orange solution in pyridine, becoming deep green on the addition of methanolic potassium hydroxide.

(*c*) The same 2 : 2′-dianthraquinonylamine was also isolated from technical 2-aminoanthraquinone by the following means. 2-Aminoanthraquinone (200 g.) was heated during 5 minutes with a boiling mixture of acetic anhydride (350 c.c.) and acetic acid (200 c.c.). On cooling, the solid was collected and heated with acetic acid (5 l.). The hot extract was separated and the residue washed with boiling acetic acid. The dark brown residue (0·4 g.) was again extracted by means of acetic acid, and then crystallised from boiling nitrobenzene. On cooling, reddish-brown prisms of 2 : 2′-dianthraquinonylamine separated (Found: N, 3·6%).

2 : 2′-*Dianthraquinonyl-N-methylamine*.—2 : 2′-Dianthraquinonylamine (1·05 g.), methyl toluene-*p*-sulphonate (4·0 g.), and dry potassium carbonate (1·0 g.) were added to trichlorobenzene (100 c.c.). The suspension was heated under reflux for 8 hours and then filtered. The orange filtrate was concentrated to small bulk; orange prisms (0·3 g.), m. p. 330°, separated on cooling. The product was sublimed at 320° (bath)/0·5 mm. An orange sublimate formed, and this was recrystallised from nitrobenzene. Small orange prisms were obtained, having m. p. 332—333° (Found: C, 78·2; H, 3·7; H, 3·3. $C_{29}H_{17}O_4N$ requires C, 78·5; H, 3·8; N, 3·2%). 2 : 2′-*Dianthraquinonyl-N-methylamine* dissolves in pyridine with an orange colour, unchanged on addition of methanolic potassium hydroxide.

1-*Chloro-2-nitroanthraquinone*.—2-Amino-1-chloroanthraquinone (30 g.; prepared by the method of Ullmann and Junghans, *Annalen*, 1913, **399**, 320) was dissolved in concentrated sulphuric acid (150 c.c.). The solution was cooled to 0°, and powdered sodium nitrite (10·2 g.) was added, with stirring, during 10 minutes. Stirring was continued for an hour, and then the solution was added to ice. The yellow precipitate was collected, washed with ice-water until the washings were only faintly acid to Congo-red, and then added to a suspension of copper sulphite in sodium nitrite; this was prepared by mixing aqueous solutions of copper sulphate (80 g.) and sodium sulphite (100 g.), collecting the brown precipitate, washing it free from sodium sulphite, and finally suspending it in water containing sodium nitrite (200 g.). Frothing occurred; this was controlled by addition of ether. After 2 hours' stirring, the product was collected and stirred with dilute hydrochloric acid. The brownish-yellow residue (34 g.; m. p. 220—240°) was extracted with *o*-dichlorobenzene (60 c.c.), and the extract treated with charcoal and filtered. On cooling, crude 1-chloro-2-nitroanthraquinone separated (yield 12 g.; m. p. 250—257°). Two recrystallisations from acetic acid gave yellow needles, m. p. 262—263° (Found: C, 58·7; H, 2·0; N, 4·7; Cl, 12·0. Calc. for $C_{14}H_6O_4NCl$: C, 58·5; H, 2·1; N, 4·9; Cl, 12·4%). Kopetschni (G.P. 363,930) records m. p. 257—258° for the quinone prepared by oxidising 2-amino-1-chloroanthraquinone

1-*Diethylamino-2-nitroanthraquinone*.—1-Chloro-2-nitroanthraquinone (0·5 g.) was heated under reflux during 30 minutes with diethylamine (25 c.c.), in the presence of potassium acetate (0·5 g.). The colour of the solution changed from yellow to deep violet-red. Water was added, and the violet *quinone* precipitated (0·55 g.) crystallised several times from acetic acid. Reddish-violet needles, m. p. 145—146°, were obtained (Found: C, 66·5; H, 4·6; N, 8·2. $C_{18}H_{16}O_4N_2$ requires C, 66·7; H, 4·9; N, 8·6%).

N-Methyl-2-nitro-1 : 2′-*dianthraquinonylamine*.—2-Nitro-1 : 2′-dianthraquinonylamine was prepared by condensing 1-chloro-2-nitroanthraquinone (10·4 g.) with 2-aminoanthraquinone (8·0 g.) by heating in trichlorobenzene during 4 hours. The deep red solution, on cooling, gave red needles, m. p. 294—295° (14·4 g.). Recrystallisation from *o*-dichlorobenzene afforded pure 2-nitro-1 : 2′-dianthraquinonylamine, m. p. 296—297° (12·2 g.). This gave a reddish-blue solution in concentrated sulphuric acid. It dissolved in pyridine with an orange-red colour which became deep green on addition of methanolic potassium hydroxide. Unlike the green colour obtained with most secondary bases of the series, that produced from 2-nitro-1 : 2′-dianthraquinonylamine is comparatively stable; it is not affected by the addition of considerable proportions of alcohol.

An attempt to prepare 2-nitro-1 : 2′-dianthraquinonylamine by heating a mixture of 1-chloro-2-nitroanthraquinone (2·9 g.), 2-aminoanthraquinone (2·25 g.), and potassium acetate (3 g.) in nitrobenzene (30 c.c.) for 3 hours gave a violet-brown product (1·8 g.), which was almost insoluble in boiling nitrobenzene. It was sparingly soluble in hot water forming a red solution, from which a yellow solid was precipitated by acid. The yellow product, crystallised several times from acetic acid, afforded glistening pale yellow plates of 1-*hydroxy-2-nitroanthraquinone*, m. p. 197—198° (Found: C, 62·4; H, 2·5; N, 4·8. $C_{14}H_7O_5N$ requires C, 62·4; H, 2·6; N, 5·2%).

1-Hydroxy-2-nitroanthraquinone was also formed when 1-chloro-2-nitroanthraquinone and 2-aminoanthraquinone were heated together in nitrobenzene solution, with the addition of copper and sodium acetate.

2-Nitro-1 : 2′-dianthraquinonylamine (10·0 g.), methyl toluene-*p*-sulphonate (10·0 g.), and dry potassium carbonate (8·0 g.) were heated together in *o*-dichlorobenzene (40 c.c.) for 8 hours. The

suspension was filtered, the residue washed by means of hot *o*-dichlorobenzene, and the washings and filtrate were combined and concentrated to small volume. On addition of ether, an orange-brown precipitate (8·2 g.; m. p. 160° with previous softening) was obtained. It was taken up in chlorobenzene and chromatographed on alumina; a dark brown, strongly adsorbed zone formed, and a main orange-red zone. Elution of the main zone by ethyl acetate and evaporation of the solvent gave orange prisms (6·1 g.), m. p. 264—265° (Found: C, 71·4; H, 3·2; N, 5·6. $C_{28}H_{14}O_4N_2$ requires C, 71·3; H, 3·3; N, 5·7%). *N-Methyl-2-nitro-1 : 2′-dianthraquinonylamine* forms an orange solution in pyridine which remains unaltered by the addition of methanolic potassium hydroxide. The solution in concentrated sulphuric acid is deep blue; addition of water precipitates a red material, which becomes orange on further dilution. Crystallisation from chlorobenzene yields dark red prisms of the *molecular compound*, $(C_{29}H_{16}O_4N_2)_2,C_6H_5Cl$, m. p. 169—170° (Found: N, 5·6; Cl, 3·6. $C_{64}H_{37}O_{12}N_4Cl$ requires N, 5·2; Cl, 3·3%). Solvents such as ether or ethyl acetate decompose the adduct, *N*-methyl-2-nitro-1 : 2′-dianthraquinonylamine, m. p. 264°, being regenerated. The nitro-amine crystallises unchanged from benzene, but dark red crystals, m. p. 160—180°, separate from its solution in *o*-dichlorobenzene. A dark red product, indistinctly crystalline, m. p. 152—168°, separates from its solution in toluene.

2-*Amino*-1 : 2′-*dianthraquinonyl*-N-*methylamine*.—(*a*) *N*-Methyl-2-nitro-1 : 2′-dianthraquinonylamine (2·0 g.) was added to a boiling solution containing stannous chloride (4·0 g.) in acetic acid (40 c.c.). After 10 minutes, the solution was cooled and mixed with water; a reddish-brown precipitate (2·0 g.), m. p. 210°, formed. This was dissolved in chlorobenzene and chromatographed on alumina. A number of brown, yellow, and red zones formed. The main zone was red, and this was eluted by ethyl acetate. Evaporation of the eluate gave the tertiary *amine* as bright red needles (0·45 g.), m. p. 306° (Found: C, 75·3; H, 3·9; N, 6·4. $C_{29}H_{18}O_4N_2$ requires C, 76·0; H, 3·9; N, 6·1%).

(*b*) *N*-Methyl-2-nitro-1 : 2′-dianthraquinonylamine (4·0 g.) was prepared in a finely divided state by dissolution in sulphuric acid (40 c.c.) and addition to water. The orange-yellow precipitate was collected, washed neutral, then added to a solution containing hydrated sodium sulphide (5·5 g.) and potassium hydroxide (5·5 g.) in water (160 c.c.). The suspension was stirred for 1 hour at 95°, then filtered, and the reddish-brown residue washed free from alkali and dried (3·0 g.; m. p. 280—290°). It was dissolved in chlorobenzene and chromatographed on alumina. The main red zone, eluted by ethyl acetate, yielded 1·4 g. of 2-amino-1 : 2′-dianthraquinonyl-*N*-methylamine as red needles, m. p. 306°. A reddish-orange zone of the column contained the unreduced nitro-compound in the form of its adduct with chlorobenzene. At the top of the column was a blue zone; this was eluted by quinoline. The blue substance dissolved in concentrated sulphuric acid with a brown colour. It dissolved in alkaline dithionite ($Na_2S_2O_4$) forming a brown solution, from which cotton was dyed; aeration gave the blue of the original colouring matter. (Cf. Part IV.)

2-*Benzamido*-1 : 2′-*dianthraquinonyl*-N-*methylamine*.—A solution containing 2-amino-1 : 2′-dianthraquinonyl-*N*-methylamine (1·2 g.) and a drop of concentrated sulphuric acid in benzoyl chloride (10 c.c.) was heated for 5 minutes under reflux, then cooled, and mixed with alcohol (30 c.c.). Orange-yellow crystals separated; these were collected and washed with alcohol (1·33 g.; m. p. 314°). Crystallisation from acetic acid, in which it was sparingly soluble, gave orange-yellow needles, m. p. 314—315° (Found: C, 76·7; H, 3·7; N, 4·9. $C_{36}H_{22}O_5N_2$ requires C, 76·9; H, 3·9; N, 5·0%). The *benzoyl* derivative dissolved in pyridine with an orange-yellow colour, becoming deep violet on addition of methanolic potassium hydroxide. The violet colour was stable towards a small proportion of water; more water reversed the colour change to yellow. The benzoyl derivative dissolved in concentrated sulphuric acid with a bright blue colour, which slowly became violet owing to hydrolysis of the benzoyl groups.

2-Amino-1 : 2′-dianthraquinonyl-*N*-methylamine was recovered unchanged after being heated for 5 hours with a solution of toluene-*p*-sulphonyl chloride in pyridine.

N-*Methyl*-2-N-*methylbenzamido*-1 : 2′-*dianthraquinonylamine*.—Methyl toluene-*p*-sulphonate (1·0 g.), 2-benzamido-1 : 2′-dianthraquinonyl-*N*-methylamine (1·0 g.), and dry potassium carbonate (0·6 g.) were heated under reflux in *o*-dichlorobenzene (20 c.c.) for 3 hours. The hot solution was filtered, and the filtrate mixed with benzene, then chromatographed on alumina. The main fraction formed an orange zone; this was eluted by acetone, and the eluate was concentrated and mixed with ether. The NN′-*dimethyl* derivative separated as orange prisms (0·2 g.), m. p. 195—196° (Found: C, 76·5; H, 4·5; N, 4·8. $C_{37}H_{24}O_5N_2$ requires C, 77·1; H, 4·2; N, 4·9%). It dissolved in pyridine with a yellow colour, unchanged by methanolic potassium hydroxide; in concentrated sulphuric acid the colour was deep blue.

N-*Methyl*-2-N-*methylamino*-1 : 2′-*dianthraquinonylamine*.—A solution containing the benzoyl derivative (0·1 g.) in concentrated sulphuric acid (2 c.c.) was heated at 100°; the colour changed from blue to violet. The solution was cooled, then added to water. An orange precipitate of the free *amine* formed (0·06 g.), having m. p. 338—340° (Found: N, 5·6. $C_{30}H_{20}O_4N_2$ requires N, 5·9%).

An attempt to prepare this derivative by methylating 2-amino-1 : 2′-dianthraquinonyl-*N*-methylamine by methyl toluene-*p*-sulphonate was unsuccessful.

NN-*Dimethylindanthrone*.—Indanthrone (Found: N, 6·3. Calc. for $C_{28}H_{14}O_4N_2$: N, 6·3%) was prepared by crystallising the sulphate from sulphuric acid and hydrolysing this with water. It was very sparingly soluble in boiling pyridine, forming a pale blue solution.

A suspension containing indanthrone (5 g.), methyl toluene-*p*-sulphonate (20 g.), and dry potassium carbonate (15 g.) in trichlorobenzene (200 c.c.) was heated under reflux during 48 hours. The suspension was filtered hot, and the green residue washed with hot trichlorobenzene. The filtrate and washings were combined and then evaporated to 40 c.c.; on cooling, violet-blue prisms having a coppery lustre separated (1·64 g.) (product A). The blue mother-liquor was mixed with benzene (300 c.c.), and then chromatographed on alumina. Development with benzene yielded the following zones in order of increasing mobility: black, pink, blue, violet, blue I, green, blue II, pale brown; a solution having a green fluorescence passed through the column.

The blue I zone was unaffected by acetone or other solvents of low b. p. Hot quinoline at 150°

eluted the blue colouring matter; it separated from the eluate during 48 hours as violet-blue crystals having a coppery lustre (0·05 g.). Its absorption spectrum in pyridine was identical with that of product A. Analysis showed it to consist of NN-*dimethylindanthrone* (Found: C, 76·2; H, 3·8; N, 5·9; NCH_3, 10·6, 11·0. $C_{28}H_{18}O_4N_2$ requires C, 76·6; H, 3·8; N, 6·0; NCH_3, 12·3%). *NN*-Dimethylindanthrone was readily soluble in pyridine with a deep blue colour. Unlike indanthrone it crystallised unaltered from solution after 0·5 g. had been heated for 200 hours under reflux with dry potassium carbonate (0·5 g.) in trichlorobenzene (10 c.c.); it was unaffected by dilute nitric acid. The solubility of *NN*-dimethylindanthrone in *o*-dichlorobenzene at 20° was 0·018 g./100 c.c.

The zone blue II was the most prominent. The colouring matter (product B) was readily eluted by acetone; the eluate on evaporation yielded bluish-violet prisms having a coppery lustre (0·19 g.) (Found: C, 77·5; H, 3·9; N, 5·6; NCH_3, 3·6; 4·2%). This product (0·1 g.) afforded a violet-blue solution in trichlorobenzene (3 c.c.), which remained unaltered on being heated with dry potassium carbonate (0·1 g.) for 150 hours. It was unaffected by dilute nitric acid.

Under other conditions the methylation of indanthrone was less satisfactory. Indanthrone (1 g.), methyl toluene-*p*-sulphonate (2 g.), and dry potassium carbonate (1·4 g.), heated under reflux for 6 hours with trichlorobenzene (100 c.c.), afforded an undissolved portion, consisting mainly of indanthrone, and a solution from which 0·2 g. of blue needles separated on filtration and cooling. This product dissolved in pyridine with a blue colour, becoming green on the addition of methanolic potassium hydroxide. The evaporated mother-liquor afforded 0·03 g. of violet-blue crystals; these dissolved in pyridine with a blue colour, rendered only slightly greener by methanolic potassium hydroxide.

Oxidation of NN-*Dimethylindanthrone.*—(*a*) *NN*-Dimethylindanthrone (0·3 g.) dissolved in concentrated sulphuric acid (6 c.c.), forming a brown solution. This was cooled to 0°, and powdered potassium nitate (0·3 g.) added; there was an immediate change in colour to bright blood-red. The mixture was stirred for 3 hours at 0°, then added to water; a blue precipitate formed. (In similar circumstances indanthrone affords a yellow oxidation product.) The suspension was made alkaline, sodium dithionite (1·0 g.) was added, and the mixture warmed to 50°. A brown solution resulted; this was filtered and the filtrate oxidised by a current of air. The precipitated blue material was easily soluble in pyridine; the colour remained unaltered when methanolic potassium hydroxide was added.

(*b*) Finely powdered *NN*-dimethylindanthrone (0·5 g.) was added at 0°, and with stirring, to nitric acid (*d* 1·4; 5·0 c.c.). After 5 minutes, fine orange-red needles separated from the yellow-brown solution. These were collected after an hour and washed by means of acetic acid; the colour changed to orange-brown. The product was insoluble in ether, alcohol, ethyl acetate, and benzene; ammonia changed it to a bluish-black material immediately. The product, dried *in vacuo* over sodium hydroxide, afforded an amorphous brownish-yellow powder (0·40 g.) (Found: C, 60·5; H, 3·1; N, 7·6, 7·9%). Heating it to 100°, or keeping it for a long period at the room temperature, caused it to become green; its yellow solution in acetic acid became green on boiling. Warming with sodium hydroxide and sodium dithionite solution reduced it, an orange solution resulting. Chromatographed on cellulose the solution afforded a thin, strongly absorbed blue zone; the remainder was removed from the column by elution with alkaline dithionite. The orange eluate, exposed to air, afforded a blue precipitate having the properties of *N*-methylindanthrone. Treatment with methyl toluene-*p*-sulphonate and potassium carbonate in trichlorobenzene reconverted it into *NN*-dimethylindanthrone.

Cyclisation of N-*Methyl*-2-N-*methylamino*-1 : 2′-*dianthraquinonylamine. Formation of* NN′-*Dimethylindanthrone.*—*N*-Methyl-2-*N*-methylamino-1 : 2′-dianthraquinonylamine was recovered unchanged after being heated with acetic acid or pyridine. The amine was readily cyclised, however, by hot methanolic potassium hydroxide. The amine (0·03 g.) was dissolved in pyridine (30 c.c.) and a solution of potassium hydroxide in methanol (0·5 c.c. of 30%) was added; there was no change in the orange colour of the solution. Heating to boiling changed the colour to olive brown and then, on shaking, to bright reddish-brown. As the shaking was continued at the b. p., the colour changed to bright green, and finally to greenish blue. The product was exposed to air for 12 hours, then mixed with methanol. The blue precipitate was collected, then washed in turn with methanol and water. The methanolic filtrate was colourless, an indication that the amine reactant was no longer present. The blue residue (0·03 g.) dissolved readily in *o*-dichlorobenzene. At 20° its solubility was 0·017 g./100 c.c. The total solubility of a mixture of the product with *NN′*-dimethylindanthrone (prepared by the direct methylation of indanthrone) was 0·018 g./100 c.c. The product was not completely homogeneous, because its blue solution in pyridine was rendered green by methanolic potassium hydroxide. A solution in *o*-dichlorobenzene chromatographed on alumina afforded two blue zones. An attempt to extract the adsorbed colouring matters by boiling *o*-dichlorobenzene resulted in the isolation of indanthrone. (Cf. Part II.)

Cyclisation of 2-*Amino*-1 : 2′-*dianthraquinonyl*-N-*methylamine. Formation of* N-*Methylindanthrone.*—(*a*) The amino-compound was recovered unaltered after 8 hours' heating with acetic acid, 16 hours' with pyridine, 12 hours' with anthracene or for 6 hours' with nitrobenzene, all at the b. p. Heating 0·1 g. of the amine with acetic anhydride (10 c.c.) for 4 hours afforded an orange product (0·1 g.), m. p. 190—200°, doubtless the *N*-acetyl derivative, which dissolved in pyridine with a yellow colour, becoming reddish-violet on addition of methanolic potassium hydroxide.

(*b*) Powdered sodium hydroxide (0·2 g.) was added to a solution of the amine (0·2 g.) in pyridine (5 c.c.). The suspension was kept at the room temperature for 10 days with occasional shaking and stirring. There was no immediate change in colour on addition of the alkali but, after 24 hours, the surface of the suspension had become green. After 10 days the whole suspension had become green; at the surface there were areas containing blue colouring matter. Methanol was added and the blue product (0·15 g.) collected. The filtrate was pale orange, an indication of the presence of unchanged amine.

(*c*) In a similar experiment in which 0·2 g. of potassium hydroxide was used, the yield of the blue colouring matter was 0·17 g.

The two blue products were combined and crystallised from quinoline; violet needles of N-*methylindanthrone* (0·17 g.) separated (Found: C, 76·4; H, 3·3; N, 5·8; NCH_3, 6·5. $C_{29}H_{14}O_4N_2$ requires C, 76·3; H, 3·5; N, 6·1; NCH_3, 6·4%). *N*-Methylindanthrone was easily soluble in hot pyridine with a deep blue colour; on addition of methanolic potassium hydroxide the colour changed immediately to green; the further addition of water or alcohol restored the original blue colour and precipitated the original blue colouring matter. *N*-Methylindanthrone dissolved in concentrated sulphuric acid with a brown colour; a blue precipitate formed immediately on addition of water. Its solubility in *o*-dichlorobenzene at 20° was 0·00076 g./100 c.c.

Oxidation of N-*Methylindanthrone.*—*N*-Methylindanthrone (0·05 g.) was stirred at 0° with nitric acid (*d* 1·4; 0·5 c.c.). It dissolved with a bright orange colour; after a short time orange needles separated (0·02 g.), identical with those obtained by the action of cold, concentrated nitric acid on *NN*-dimethylindanthrone. The product dissolved in alkaline dithionite forming a brown solution; on exposure to air the solution re-formed *N*-methylindanthrone.

Methylation.—*N*-Methylindanthrone (20 mg.), methyl toluene-*p*-sulphonate (40 mg.) and dry potassium carbonate (20 mg.) were heated under reflux during 8 hours with *o*-dichlorobenzene (3 c.c.). The suspension was filtered while hot, cooled, mixed with benzene, and chromatographed on alumina; a single, uniform, blue zone resulted. The colouring matter was eluted by means of quinoline and the eluate evaporated to a small volume. The characteristic coppery-blue crystals of *NN*-dimethylindanthrone (12 mg.) separated. The product dissolved in pyridine with a blue colour which remained unaltered on adding methanolic potassium hydroxide. Its absorption spectrum in pyridine was identical with that of *NN*-dimethylindanthrone prepared by methylation of indanthrone. The solubility in *o*-dichlorobenzene was 0·029 g./100 c.c. at 20°. The solubility of a mixture of the product with *NN*-dimethylindanthrone, prepared by the methylation of indanthrone, was 0·026 g./100 c.c.

2-Amino-1 : 2′-dianthraquinonylmethylamine (0·2 g.) was recovered unaltered when its solution in pyridine (5 c.c.) was shaken at intervals during 10 days with lithium hydroxide (0·2 g.), and methyl alcohol was subsequently added. A slight green colour developed after 3 days.

2-N-*Methylacetamidoanthraquinone.*—2-Methylaminoanthraquinone (1·0 g.) was heated under reflux for an hour with acetic acid (10 c.c.) containing acetic anhydride (10 c.c.). The orange precipitate, obtained on adding the mixture to water, crystallised from alcohol (charcoal) in pale yellow needles (0·6 g.), m. p. 159—160° (Found: C, 72·8; H, 4·7; N, 5·2. $C_{17}H_{13}O_3N$ requires C, 73·1; H, 4·7; N, 5·0%). The pale yellow solution of the *acetyl* derivative in pyridine remained unchanged in colour on addition of methanolic potassium hydroxide.

Potassium Salt of 2-*Benzamidoanthraquinone.*—A solution containing potassium hydroxide (0·2 g.) in methyl alcohol (0·6 c.c.) was added to one containing 2-benzamidoanthraquinone (0·5 g.) in pyridine (10 c.c.). The deep red-violet solution was added to benzene (500 c.c.); a flocculent precipitate separated. This was filtered off; the filtrate was yellow, owing to the presence of excess of the benzoyl derivative. The residue, after drying *in vacuo*, consisted of bluish-red flakes (0·45 g.) (Found: N, 3·8; K, 10·8. $C_{21}H_{12}O_3NK$ requires N, 3·8; K, 10·7%). The *potassium* salt dissolved in pyridine with a reddish-violet colour, becoming orange and then yellow on addition of methanol. It darkened at 160° and melted at 246—250°. Apparently, fusion occurred without decomposition, because the fused salt dissolved in pyridine with a violet colour rendered yellow on adding water. On exposure to air the colour of the salt became yellow; at the same time potassium carbonate was formed.

An attempt to methylate the potassium salt (3·0 g.) by methyl iodide (10 c.c.) at 120—130° for 24 hours gave only 2-benzamidoanthraquinone.

2-N-*Methylbenzamidoanthraquinone.*—(*a*) 2-Methylaminoanthraquinone (1·0 g.) was heated with benzoyl chloride (2 c.c.) in pyridine (20 c.c.) for 30 minutes. The *benzoyl* derivative crystallised from aqueous acetic acid in bright orange-yellow needles (0·45 g.), m. p. 171—172° (Found: C, 77·4; H, 4·2; N, 4·2. $C_{22}H_{15}O_3N$ requires C, 77·3; H, 4·4; N, 4·1%). There was no change in colour on addition of methanolic potassium hydroxide to its yellow solution in pyridine.

(*b*) 2-Benzamidoanthraquinone (1·0 g.), methyl toluene-*p*-sulphonate (1·0 g.), and dry potassium carbonate (0·6 g.) were heated together in *o*-dichlorobenzene (20 c.c.) for 5 hours. The suspension was filtered, and the filtrate evaporated to a small volume, and then mixed with ether; pale yellow crystals (0·47 g.), m. p. 165—168°, separated. This product was dissolved in benzene and chromatographed on alumina. Two zones formed; the more strongly adsorbed was 2-benzamidoanthraquinone. The yellow, less strongly adsorbed, zone was eluted with acetone and the eluate evaporated. Orange-yellow crystals, m. p. 172—173°, were obtained, the m. p. of which was not depressed by admixture with authentic 2-*N*-methylbenzamidoanthraquinone. The methylated product dissolved in pyridine with a yellow colour, which was not affected by methyl alcoholic potassium hydroxide.

2-p-*Nitrobenzamidoanthraquinone.*—2-Aminoanthraquinone (2·0 g.) was heated under reflux for 30 minutes with pyridine (10 c.c.) containing *p*-nitrobenzoyl chloride (4 g.). The colour of the solution changed from orange to yellow; on addition of alcohol the p-*nitrobenzoyl* derivative (2·5 g.) crystallised. It separated from nitrobenzene in bunches of pale yellow needles (1·7 g.), m. p. 303—304° (Found: C, 67·6; H, 3·1; N, 7·2. $C_{21}H_{12}O_5N_2$ requires C, 67·7; H, 3·2; N, 7·5%). 2-*p*-Nitrobenzamidoanthraquinone dissolved in pyridine with a pale yellow colour which became deep red-violet on addition of methyl alcoholic potassium hydroxide and pale orange on the further addition of methyl alcohol.

Potassium salt. This *derivative* was obtained as a red powder (Found: N, 6·4; K, 9·5. $C_{21}H_{11}O_5N_2K$ requires N, 6·8; K, 9·5%) by treating potassium hydroxide with 2-*p*-nitrobenzamidoanthraquinone by the method adopted for the analogous derivative of 2-benzamidoanthraquinone. It dissolved in pyridine with a red colour; it was more stable towards hydrolysis than the un-nitrated salt.

2-N-*Methyl*-p-*nitrobenzamidoanthraquinone.*—Prepared similarly by heating 2-methylaminoanthraquinone (1·0 g.) with *p*-nitrobenzoyl chloride (2·0 g.) in pyridine (20 c.c.) for an hour, this *amide*

crystallised from acetic acid in pale yellow needles (0·55 g.), m. p. 233° (Found: C, 68·0; H, 4·1; N, 7·3. $C_{22}H_{14}O_4N_2$ requires C, 68·4; H, 3·6; N, 7·3%). Its pale yellow solution in pyridine remained unaltered in colour on addition of methanolic potassium hydroxide.

2-N-*Methylacetamido*-1-*nitroanthraquinone*.—2-Acetamido-1-nitroanthraquinone (10 g.; Ullmann and Medenwald, *Ber.*, 1913, **46**, 1798) was added to 500 c.c. of 5% sodium hydroxide solution and warmed to 60—70°. The orange solution was filtered, leaving a residue of 2-amino-1-nitroanthraquinone, m. p. 306°. The red filtrate was stirred for 30 minutes with methyl sulphate (20 c.c.); an orange precipitate formed (6·8 g.), having m. p. 247°. Several recrystallisations from acetic acid afforded glistening pale yellow plates (3·3 g.), m. p. 260—261° (Found: C, 62·6; H, 3·6; N, 8·2. $C_{17}H_{12}O_4N_2$ requires C, 62·9; H, 3·7; N, 8·6%). The *methyl* derivative dissolved in pyridine with a pale yellow colour which remained unchanged on adding methanolic potassium hydroxide

2-*Methylamino*-1-*nitroanthraquinone*.—A solution containing 1·0 g. of 2-*N*-methylacetamido-1-nitroanthraquinone in 10 c.c. of concentrated sulphuric acid was heated at 100° for 1 hour and then added to water; an orange precipitate (0·65 g.; m. p. 218—230°) formed. Crystallisation from alcohol afforded orange needles of 2-*methylamino*-1-*nitroanthraquinone* (0·2 g.), m. p. 246° (Found: C, 63·7; H, 3·5; N, 9·9. $C_{15}H_{10}O_4N_2$ requires C, 63·8; H, 3·6; N, 9·9%). It dissolved in pyridine forming an orange solution which became pale green on addition of methanolic potassium hydroxide. The intensity of the green colour was much less than that characteristic of 2-amino-1-nitroanthraquinone.

2-*Benzamido*-1-*nitroanthraquinone*.—Concentrated sulphuric acid (2—3 drops) was added at 100° to a solution containing 2-amino-1-nitroanthraquinone (3·0 g.) in benzoyl chloride (20 c.c.). The solution was agitated for an hour and then mixed with alcohol. The *benzoyl* derivative separated (4·7 g.; m. p. 235—240°). Crystallisation from acetic acid (charcoal) afforded long, pale yellow needles (3·4 g.), m. p. 246—247° (Found: C, 67·8; H, 3·1; N, 7·6. $C_{21}H_{12}O_4N_2$ requires C, 67·7; H, 3·2; N, 7·5%).

2-N-*Methylbenzamido*-1-*nitroanthraquinone*.—2-Benzamido-1-nitroanthraquinone (2·0 g.) was added to 5% sodium hydroxide solution (200 c.c.) and warmed to 80°. The deep-red solution was filtered, and the filtrate stirred for 2 hours with methyl sulphate (12 c.c.). The orange-yellow precipitate was collected and extracted by dilute sodium hydroxide solution until the extract was colourless; finally it was washed by means of water and dried. The *methylamide* (1·1 g.; m. p. 228—230°) crystallised from acetic acid in fine, pale yellow needles (0·6 g.), m. p. 231—232° (Found: C, 68·8; H, 3·4; N, 7·0. $C_{22}H_{14}O_4N_2$ requires C, 68·4; H, 3·6; N, 7·3%). This product dissolved in pyridine with a very pale yellow colour; there was no change on addition of methanolic potassium hydroxide. Hydrolysis with concentrated sulphuric acid gave orange needles of 2-methylamino-1-nitroanthraquinone, m. p. 246—247°, not depressed when mixed with an authentic specimen.

2-*Dimethylaminoanthraquinone*.—2-Chloroanthraquinone (4·0 g.), potassium acetate (4·0 g.), copper bronze (0·1 g.), cupric acetate (0·1 g.), and aqueous dimethylamine (24 c.c. of 33%) were heated for 2 hours at 200°. The red product crystallised from glacial acetic acid in fine, orange-red needles (3·5 g.), m. p. 185—186° (Found: C, 76·5; H, 5·3; N, 5·6. Calc. for $C_{16}H_{13}O_2N$: C, 76·5; H, 5·2; N, 5·6%). Haller and Cryot (*Bull. Soc. chim.*, 1901, **25**, 206) obtained this compound by cyclising *o*-4-dimethylaminobenzylbenzoic acid and oxidising the product; they recorded m. p. 181°. The yellow solution of 2-dimethylaminoanthraquinone in pyridine was unaltered on addition of methanolic potassium hydroxide.

2-*Anilinoanthraquinone*.—This was obtained as golden-orange plates, m. p. 238—239°, by treating 2-chloroanthraquinone with aniline in the presence of copper bronze, cupric acetate, and potassium acetate (G.P. 288,464 records m. p. 234—236°).

The following experiment was carried out with the object of finding a more convenient preparation of 2-anilinoanthraquinone. Sodamide (4·0 g.) and aniline (50 c.c.) were heated to 150°, the liberated ammonia being removed under reduced pressure. A solution containing 2-chloroanthraquinone (5 g.) in aniline (50 c.c.) was then added; the mixture became greenish. It was heated under reflux at 150°, under reduced pressure, for 30 minutes, then cooled, and carefully mixed with water. Aniline was removed by distillation in steam, the green residue (5 g.) dissolved in benzene, and the solution chromatographed on alumina. A yellow zone was weakly adsorbed and easily eluted from the column by benzene; it consisted of 2-chloroanthraquinone. The main zone was blue; elution with acetone and evaporation of the extract afforded a residue which crystallised from acetic acid in blue needles having a coppery lustre (0·45 g.), m. p. 236—237° (Found: C, 79·8; H, 4·3; N, 6·7; Cl, 0·1. Calc. for $C_{28}H_{18}O_2N_2$: C, 80·4; H, 4·1; N, 7·2%). The product dissolved in pyridine with a reddish-blue colour which was little affected by adding methanolic potassium hydroxide. Its solution in concentrated sulphuric was greenish-yellow, becoming green on adding water; subsequently a blue precipitate formed. It dissolved in alkaline dithionite, forming a reddish-brown solution.

Sodium salt. A solution of sodioanthracene in ether was prepared by shaking a suspension of anthracene (3 g.) and powdered sodium (4 g.) in dry ether (250 c.c.). The blue solution was filtered into one of 2-anilinoanthraquinone (0·3 g.) in dry ether; a green precipitate formed. The green product was filtered off, and then brought into contact with methyl iodide. (All these operations were carried out in nitrogen free from oxygen.) The methylation product did not appear to contain 2-*N*-methylanilinoanthraquinone. In another experiment the green sodio-derivative was exposed to air; it became brown, the decomposed product dissolving in pyridine with an orange colour and then affording a green solution on the addition of methanolic potassium hydroxide.

2-*Acetanilidoanthraquinone*.—2-Anilinoanthraquinone (0·5 g.) potassium acetate (2·0 g.) and acetyl chloride (20 c.c.) were heated under reflux for 3 hours; the colour of the solution changed from orange to yellow. The product was mixed with methyl alcohol, and potassium acetate was added until the suspension was neutral to Congo-red. The filtered solution was evaporated almost to dryness, then mixed with water, and the sticky precipitate crystallised from methyl alcohol (charcoal). The product (0·1 g.) was obtained as pale yellow needles, m. p. 131° (Found: N, 4·1. $C_{22}H_{15}O_3N$ requires N, 4·1%)

It dissolved in pyridine with a yellow colour; methanolic potassium hydroxide changed the colour to green almost immediately as a result of hydrolysis.

2-*Benzanilidoanthraquinone*.—2-Anilinoanthraquinone (0·5 g.), benzoyl chloride (5 c.c.), and pyridine (3 c.c.) were heated together under reflux for an hour. Alcohol was added; the *benzoyl* derivative (0·2 g.; m. p. 155—156°) separated very slowly. Recrystallisation from alcohol gave silvery grey needles, m. p. 159—160° (Found: C, 79·9; H, 4·3; N, 3·4. $C_{27}H_{17}O_2N$ requires C, 80·3; H, 4·2; N, 3·5%). The yellow solution in pyridine showed no immediate change on addition of methanolic potassium hydroxide, but a deep-green colour gradually developed, and addition of water then precipitated 2-anilinoanthraquinone, m. p. 235—236°. The benzoyl derivative dissolved in concentrated sulphuric acid with an orange-red colour; warming brought about a blue colour as a result of hydrolysis to 2-anilinoanthraquinone.

2-N-*Methylanilinoanthraquinone*.—2-Anilinoanthraquinone (10 g.), methyl toluene-*p*-sulphonate (12·5 g.), and dry potassium carbonate (6·7 g.) were heated under reflux for 5 hours in *o*-dichlorobenzene (80 c.c.). The suspension was filtered hot, the residue washed by *o*-dichlorobenzene, and the combined washings and filtrate were evaporated to 30 c.c. and then mixed with ligroin. An orange product separated (8·6 g.; m. p. 160°). Crystallisation from alcohol gave the tertiary *amine* as orange needles (7·5 g.), m. p. 163—164° (Found: C, 80·3; H, 4·5; N, 4·5. $C_{21}H_{15}O_2N$ requires C, 80·5; H, 4·8; N, 4·5%). The orange solution in pyridine was unaffected by methanolic potassium hydroxide.

Potassium salt of 2-*Toluene*-*p*-*sulphonamidoanthraquinone*.—2-Toluene-*p*-sulphonamidoanthraquinone (38 g.) was dissolved in a hot solution containing potassium hydroxide (10 g.) in water (500 c.c.). The red solution was filtered; on cooling, the *potassium* salt separated (35 g.). It crystallised from 95% alcohol in bluish-red rhombs (Found: C, 60·2; H, 3·7; N, 3·3; S, 7·3; K, 10·0. $C_{21}H_{14}O_4NSK$ requires C, 60·6; H, 3·4; N, 3·4; S, 7·7; K, 9·4%).

Heating the potassium salt (9·0 g.) with ethyl iodide (10 c.c.) at 110° for 24 hours gave 7 g. of an alkali-insoluble product, m. p. 139°. Crystallisation from alcohol gave pale yellow needles of *N-ethyltoluene*-p-*sulphonamidoanthraquinone*, m. p. 139—140° (5·4 g.) (Found: C, 68·0; H, 4·6; N, 3·7; S, 8·2. $C_{23}H_{19}O_4NS$ requires C, 68·1; H, 4·7; N, 3·5; S, 7·9%). Warming the *N*-ethyl derivative (6 g.) with concentrated sulphuric acid (50 c.c.) at 100° for 30 minutes and adding the resulting solution to water gave 3·9 g. of an orange precipitate, m. p. 198—199°. Crystallisation from acetic acid gave orange needles of 2-ethylaminoanthraquinone (3·5 g.), m. p. 198—199° (Found: C, 76·4; H, 5·3; N, 5·9. Calc. for $C_{16}H_{13}O_2N$: C, 76·5; H, 5·2; N, 5·6%). This derivative dissolved in pyridine with a yellow colour, unchanged by methanolic potassium hydroxide. Marcinków and Piażek (*Rocz. Chem.*, 1936, **16**, 395) claim to have prepared this compound by the action of ethylamine on 2-chloroanthraquinone, but do not record the m. p.

The potassium salt (5 g.) did not appear to react with *n*-butyl bromide at 110° during 48 hours. Heated further at 150° for 24 hours, and then extracted by means of aqueous sodium hydroxide, it gave an alkali-insoluble product (4·9 g.; m. p. 144—146°). This crystallised from acetic acid in stout yellow prisms of 2-N-n-*butyltoluene*-p-*sulphonamidoanthraquinone* (2·3 g.), m. p. 147° (Found: C, 69·0; H, 5·3; N, 3·2; S, 7·0. $C_{25}H_{23}O_4NS$ requires C, 69·3; H, 5·3; N, 3·2; S, 7·4%). There was no change in the yellow colour of a solution of this derivative in pyridine on addition of methanolic potassium hydroxide.

1-*Chloro*-2-*toluene*-p-*sulphonamidoanthraquinone*.—A solution containing 2-amino-1-chloroanthraquinone (100 g.) and toluene-*p*-sulphonyl chloride (80 g.) in pyridine (500 c.c.) was heated under reflux for 4 hours. One-half of the pyridine was then distilled off, and alcohol was added to the residue. The yellow product which separated was collected, washed with alcohol (yield, 131 g.; m. p. 205°), and recrystallised from acetic acid. Fine yellow needles separated, having m. p. 208—209° (Found: C, 61·2; H, 3·5; N, 3·4; Cl, 9·0; S, 7·9. Calc. for $C_{21}H_{14}O_4NClS$: C, 61·2; H, 3·4; N, 3·5; Cl, 8·6; S, 7·8%). The compound has been prepared (G.P. 376,471) by heating 2-toluene-*p*-sulphonamidoanthraquinone with sulphuryl chloride and borax.

The *potassium* derivative was obtained by adding 8·2 g. of the amide to a warm solution of potassium hydroxide (1·7 g.) in water (100 c.c.). A red tarry product was formed, but this became granular as the temperature was raised to the b. p. Having been filtered off, washed and dried, the product (7·5 g.) was crystallised from ethyl alcohol, in which it was sparingly soluble. It formed reddish-orange prisms, m. p. above 300° (Found, in material dried *in vacuo*: C, 56·0; H, 3·0; N, 3·1; Cl, 8·3; S, 6·9; K, 9·4. $C_{21}H_{13}O_4NClSK$ requires C, 56·0; H, 2·9; N, 3·1; Cl, 7·9; S, 7·1; K, 8·7%).

1-*Chloro*-2-N-*methyltoluene*-p-*sulphonamidoanthraquinone*.—This *derivative* resulted when the potassium salt (15 g.) was heated at 100—110° for 24 hours with methyl iodide (15 c.c.). The product was extracted with hot sodium hydroxide solution, and the insoluble portion (13·7 g.) dried and recrystallised from acetic acid. It formed yellow needles (11·2 g.), m. p. 209° (Found: C, 61·8; H, 3·9; N, 3·3; Cl, 8·8; S, 7·8. $C_{22}H_{16}O_4NClS$ requires C, 62·0; H, 3·8; N, 3·3; S, 7·5; Cl, 8·3%).

1-*Chloro*-2-*methylaminoanthraquinone*.—The toluene-*p*-sulphonyl derivative (10 g.) was heated at 95° for an hour with concentrated sulphuric acid (50 c.c.), and the resulting solution added to water. The precipitate, collected, washed, dried, and crystallised from acetic acid, gave 6·3 g. of orange needles, m. p. 240° (Found: C, 66·4; H, 3·5; N, 4·8; Cl, 12·9. $C_{15}H_{10}NCl$ requires C, 66·5; H, 3·7; N, 5·2; Cl, 13·1%). This *quinone* dissolved in pyridine with an orange colour; methanolic potassium hydroxide caused a faint, but distinct, green coloration. It was shown that this could not be due to small amounts of 2-amino-1-chloroanthraquinone.

1-*Chloro*-2-N-*methylacetamidoanthraquinone*.—A suspension containing 1-chloro-2-methylaminoanthraquinone (0·5 g.) and potassium acetate (1 g.) in acetyl chloride (10 c.c.) was heated under reflux until a pale yellow solution resulted. The *acetyl* derivative, precipitated by addition of the mixture to water and recrystallised from alcohol, gave pale yellow needles (0·2 g.), m. p. 204—205° (Found: N, 4·7; Cl, 11·7. $C_{17}H_{12}O_2NCl$ requires N, 4·5; Cl, 11·3%). It dissolved in pyridine with a yellow colour, unaltered by methanolic potassium hydroxide.

1-*Chloro*-2-*ditoluene*-p-*sulphonylaminoanthraquinone*.—2-Amino-1-chloroanthraquinone (7 g.), toluene-*p*-sulphonyl chloride (7 g.), and pyridine (40 c.c.) were heated under reflux for 4 hours. The resulting solution was mixed with alcohol, and the pale yellow product (11·5 g.), m. p. 250—260°, was extracted with a solution containing potassium hydroxide (4 g.) in alcohol–water (100 : 200 c.c.). The residual 2-*disulphonylamino-quinone* (7 g.) crystallised from nitrobenzene in pale yellow needles (5·9 g.), m. p., 297—298° (Found : C, 59·8; H, 3·8; N, 2·7; Cl, 6·5; S, 11·5. $C_{28}H_{20}O_6NClS_2$ requires C, 59·4; H, 3·5; N, 2·5; Cl, 6·3; S, 11·3%). It was sparingly soluble in acetic acid. The yellow colour of its solution in pyridine remained unaffected by methyl alcoholic potassium hydroxide.

2-*Benzamido*-1-*chloroanthraquinone*.—2-Amino-1-chloroanthraquinone (5 g.), benzoyl chloride (10 c.c.), and pyridine (20 c.c.) were heated under reflux for 10 minutes, then cooled, and mixed with alcohol. The *benzamido*-derivative which separated (4·3 g.) was crystallised twice from acetic acid; it formed fine pale yellow needles (3·1 g.), m. p. 219—220° (Found : C, 70·0; H, 3·6; N, 4·2; Cl, 10·0. $C_{21}H_{12}O_3NCl$ requires C, 69·8; H, 3·3; N, 3·9; Cl, 9·9%).

2-*Chloro*-1-*nitroanthraquinone*.—Nitric acid (*d* 1·35; 55 c.c.) was added with stirring to a solution containing 2-chloroanthraquinone (25 g.) in concentrated sulphuric acid (135 c.c.), the temperature being kept below 10°. Yellow crystals separated; after 5 hours these were collected and washed by means of water. The *nitro-quinone* (15 g.; m. p. 190—210°), crystallised from *o*-dichlorobenzene and then from acetic acid, had m. p. 280—281° (Found : N, 4·6; Cl, 12·9. $C_{14}H_6O_4NCl$ requires N, 4·9; Cl, 12·4%). The yield of pure material was 3·5 g.

1-*Anilino*-2-*chloroanthraquinone*.—2-Chloro-1-nitroanthraquinone (1·0 g.), potassium acetate (1·0 g.), copper bronze (0·02 g.), cupric acetate (0·02 g.), and aniline (20 c.c.) were heated under reflux for 6 hours. The product was distilled in steam, the violet residue (1·25 g.) dissolved in benzene, and the solution chromatographed on alumina. A weakly adsorbed violet zone resulted; this was eluted by benzene and recovered (0·52 g.; m. p. 196—197°). Crystallisation from acetic acid gave the *base* as violet needles, m. p. 204—205° (Found : C, 71·2; H, 3·8; N, 4·4; Cl, 10·6. $C_{20}H_{12}O_2NCl$ requires C, 71·6; H, 3·6; N, 4·2; Cl, 10·6%). Like 1-anilinoanthraquinone the product dissolved in pyridine with a violet colour which was unaltered by methyl alcoholic potassium hydroxide.

2-*Nitroanthraquinone*.—An ice-cold solution containing 2-aminoanthraquinone (10 g.) in concentrated sulphuric acid (70 c.c.) was added during an hour to a stirred solution containing ammonium persulphate (50 g.) in water (200 c.c.), at <5°. The addition being complete, stirring was continued at 5° for an hour, then at 90° for 2 hours; the colour of the suspension changed from orange to dull yellow. The solid was collected, washed acid-free, and dried (9·3 g.; m. p. 157—166°). Extraction with acetic acid (100 c.c.) gave a solution from which orange-brown crystals (5 g.; m. p. 176—177°) separated. Repeated crystallisation from acetic acid afforded 1·3 g. of bright yellow plates of 2-nitroanthraquinone, m. p. 183—184° (Found : C, 66·2; H, 2·7; N, 5·6. Calc. for $C_{14}H_7O_4N$: C, 66·4; H, 2·8; N, 5·5%). The material (0·5 g.; m. p. 330—335°) insoluble in acetic acid separated in indistinct crystals, m. p. 335—340° (decomp.) (Found : C, 73·3; H, 3·0; N, 6·1. Calc. for $C_{28}H_{14}O_5N_2$: C, 73·4; H, 3·1; N, 6·1%). This product (2 : 2′-azoxyanthraquinone) dissolved in concentrated sulphuric acid with an orange-brown colour; a pale yellow precipitate formed on addition of water. Warming with acetone and methanolic potassium hydroxide gave a dull blue colour (cf. Scholl and Eberl, *Monatsh.*, 1911, **32**, 1035).

Fusion of 2-Nitroanthraquinone with Potassium Hydroxide. Formation of Alizarin.—2-Nitroanthraquinone (1·0 g.) and potassium hydroxide (10 g.) were powdered together, water (4 c.c.) was added, and the mixture heated. At 120° the mixture became fluid and deep green, at 160—180° it became violet. The product was cooled and added to water, and air was passed through the resulting solution. The violet solution was filtered (there was only a trace of a residue), and the filtrate acidified. The orange-brown precipitate (0·6 g.; m. p. 270—280°), crystallised from acetic acid in orange-brown needles, m. p. 289—290°, not depressed on admixture with alizarin.

Fusion of 2-Anilinoanthraquinone with Potassium Hydroxide.—(a) *At 180°, in the presence of oxidants*. A finely powdered mixture of 2-anilinoanthraquinone (10 g.), anhydrous potassium acetate (5·0 g.), and potassium nitrate (1·2 g.) was added during 10 minutes to a melt containing potassium hydroxide (30 g.) and water (4 c.c.) at 180°. An even temperature was secured by carrying out the fusion in a nickel crucible immersed in a fusible-metal bath. The first portions of 2-anilinoanthraquinone dissolved with a green colour, which quickly changed to blue. The smell of aniline was noticed. The addition being complete, the melt was stirred at 180—190° for 30 minutes, during which it acquired a coppery lustre; considerable frothing occurred. The melt was added to water containing ice, a solution containing concentrated sulphuric acid (8 c.c.) in water was added, and the still alkaline solution was heated to 100° and then aerated for 2 hours. Filtration afforded a violet residue (A); this was washed by water. The filtrate from (A) was acidified and the resulting brownish-yellow gelatinous precipitate was collected and dried (3·8 g.; m. p. 282—283°). Recrystallisation from acetic acid gave brownish-yellow needles, m. p. 287—288°, not depressed by mixing them with alizarin, m. p. 289°. Acetylation afforded 2-acetylalizarin, m. p. 203°. Methylation by potassium hydroxide and methyl sulphate gave alizarin 2-methyl ether, m. p. 228—229°.

The violet product (A) (5·9 g.; m. p. >300°) dissolved in concentrated sulphuric acid with an olive green colour; warming changed the colour to blue; a reddish-violet precipitate formed on addition of the solution to water. The material (A) was sparingly soluble in 1% aqueous potassium hydroxide; ultimately a solution was obtained which, acidified, yielded a violet product (1·1 g.), probably 2-*anilino*-1-*hydroxyanthraquinone*. This dissolved in glacial acetic acid forming a red solution, from which it separated in violet prisms, m. p. 225—226° (Found : C, 75·6; H, 4·3; N, 4·3. $C_{20}H_{13}O_3N$ requires C, 77·1; H, 4·0; N, 4·3%). It dissolved in hot aqueous potassium hydroxide; on cooling, a violet potassium salt separated, identical with the main constituent of the residue (A). It dissolved in pyridine with a red colour; addition of methanolic potassium hydroxide changed the colour to blue; a violet solution resulted when water was added. Heating with a mixture of boric anhydride and acetic anhydride changed

the colour to greenish-blue; addition of chloroform yielded a green solution, but further addition changed the colour to violet-brown.

There was no evidence of unchanged 2-anilinoanthraquinone amongst the products.

(b) *At* 200—210°, *in the presence of oxidants.* Experiment (*a*) was repeated at 200—210°; the period of fusion was 40 minutes. The products were crude alizarin (6·0 g.) and the violet product A (3·5 g.). From the latter was prepared the violet derivative, m. p. 223—224° (2·2 g.).

(c) *At* 180—200°, *in the presence of phenol.* 2-Anilinoanthraquinone (10 g.) was added to 180° to a melt consisting of potassium hydroxide (34 g.), water (6 g.), and phenol (6 g.). The mass was stirred for 45 minutes, during which the temperature was allowed to rise to 200°; there was little tendency to froth. The product was added to water and aerated for several hours. The resulting suspension was filtered; the violet filtrate on acidification gave alizarin (4·5 g.) as a bright orange-yellow precipitate; it crystallised from acetic acid in brownish needles, m. p. 289°, alone or when mixed with an authentic sample. The residue remaining after separation of the violet filtrate was red; most of it (4·2 g.) was soluble in hot benzene and separated on cooling as orange-brown crystals (3·0 g.) of 2-anilinoanthraquinone, m. p. 233—235°. A portion of the residue (0·7 g.) did not dissolve in benzene; this crystallised from acetic acid in violet-blue prisms, m. p. 222° (0·2 g.), identical with the product of m. p. 225—226° obtained by the alkali fusion of 2-anilinoanthraquinone in the presence of an oxidant.

Potassium hydroxide fusion of product, m. p. 225—226°. The product, m. p. 225—226° (0·5 g.), was added at 200° to a melt of potassium hydroxide (5 g.) and water (1 c.c.), and the mixture was stirred for 15 minutes; there was little evidence of reaction. Finally, the temperature was raised to 240—250°, and then the melt was added to water. The violet solution was filtered from the undissolved material (0·35 g.); the residue separated from acetic acid in violet crystals, m. p. 224—225°, identical with the starting material. The violet filtrate, acidified, yielded 0·1 g. of a reddish-violet precipitate, m. p. 204—220°.

Fusion of 2-N-*Methylanilinoanthraquinone with Potassium Hydroxide.*—A finely powdered mixture of 2-*N*-methylanilinoanthraquinone (5·0 g.), potassium nitrate (0·6 g.), and potassium acetate (2·5 g.) was added during 10 minutes to a melt of potassium hydroxide (15 g.) and water (2 c.c.). There was no apparent reaction. After 30 minutes' stirring, the melt was added to water, and the suspension heated to boiling, aerated, and filtered. The pale violet filtrate gave on acidification a red-violet precipitate, m. p. 130—150°. The residue (4·5 g.), m. p. 145°, was extracted by benzene until nothing more dissolved; a residue (0·5 g.) remained.

The residue was a potassium salt; it reacted with acetic acid and the product, 2-N-*methylanilinoanthraquinone*, crystallised from the solvent in red-brown needles (0·2 g.), m. p. 200—205° (Found: C, 75·9; H, 4·8; N, 3·8. $C_{21}H_{15}O_2N$ requires C, 77·4; H, 4·4; N, 4·1%). This compound dissolved in pyridine with a red colour; addition of methanolic potassium hydroxide changed the colour to violet-blue, and this was stable on further addition of water.

The benzene solution, chromatographed on alumina, afforded three main zones. Most strongly adsorbed was a blue substance. This could not be eluted by means of acetone; it dissolved in concentrated sulphuric acid, forming a deep green solution from which a violet precipitate separated on addition of water. The violet product (0·05 g.) had m. p. 200°; it was identical with the substance, m. p. 200—205°, obtained by treating the benzene-insoluble residue with acetic acid.

The second zone was eluted by means of acetone; on evaporation the eluate afforded orange-brown needles (0·15 g.), m. p. 235°, not depressed by mixing it with authentic 2-anilinoanthraquinone. The product also showed the reactions of 2-anilinoanthraquinone including the development of a deep green colour on addition of methanolic potassium hydroxide to its orange solution in pyridine. (The 2-*N*-methylanilinoanthraquinone employed in this experiment was free from 2-anilinoanthraquinone.)

The least strongly adsorbed zone was red. Elution with benzene and evaporation of the eluate afforded 3·02 g. of fine red needles, m. p. 157—161°; after recrystallisation from alcohol the m. p. was 163°, not depressed by mixing the product with 2-*N*-methylanilinoanthraquinone.

Condensation of 2-*Aminoanthraquinone with Nitrobenzene.*—The preparation was carried out as outlined in F.I.A.T. Final Report 1313, Vol. III, p. 82. The *product* was obtained by crystallisation from nitrobenzene as yellow needles having a coppery lustre, m. p. 356—357° (Found: C, 70·1; H, 3·8; N, 7·9. $C_{20}H_{12}O_4N_2$ requires C, 69·8; H, 3·5; N, 8·1%). It dissolved in pyridine with an orange colour changed to deep violet by a drop of methanolic potassium hydroxide, and green, finally orange, by further addition of methanol. It dissolved in concentrated sulphuric acid with a deep blue colour.

2-p-*Nitroanilinoanthraquinone.*—2-Chloroanthraquinone (9·6 g.), *p*-nitroaniline (7·2 g.), potassium carbonate (5·5 g.), cupric acetate (0·5 g.) and copper bronze (0·2 g.) were heated under reflux in nitrobenzene (100 c.c.) for 3 hours. The resulting suspension was filtered hot; on cooling the filtrate afforded pale brown crystals (6·7 g.; m. p. *ca.* 208°). The crystals were extracted by acetic acid; a brown residue remained, having m. p. >300°. Crystallised from nitrobenzene (charcoal), the residue afforded microscopic yellow needles having a coppery lustre (1·1 g.), m. p. 357°, not depressed by mixing it with the product obtained by condensing 2-aminoanthraquinone with nitrobenzene. The colour reactions of the two products were identical.

The authors thank the University of Leeds for the award of a Clothworkers Research Scholarship, and the Trustees of Messrs. Courtaulds' Scientific and Educational Trust Fund for the award of a grant to one of them (E. L.). They also thank Imperial Chemical Industries Limited for gifts of intermediates and grants to meet the cost of microanalyses.

CLOTHWORKERS RESEARCH LABORATORY,
UNIVERSITY OF LEEDS.

[*Received, February 27th,* 1951.]

471. *Chemistry of Indanthrone. Part II.* The Formation of Dianthraquinonyl-N-methylamines.*

By William Bradley and Edward Leete.

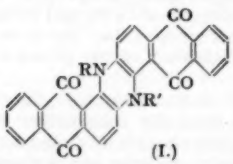
An attempt to prepare *NN*-dimethylindanthrone by the self-condensation of 2-bromo-1-methylaminoanthraquinone yielded *N*-methylindanthrone. It was then found that both 2-bromo-1-methylaminoanthraquinone and *NN*-dimethylindanthrone were readily demethylated when heated in nitrobenzene with copper or its salts and an alkali, formaldehyde being liberated. 1-Chloro-2-methylaminoanthraquinone afforded 2-methylaminoanthraquinone, 2-aminoanthraquinone, and the cuprous derivative (A) of *NN*-di-2-anthraquinonylformamidine (B), dehalogenation, demethylation, and further condensation having occurred. The cuprous derivative (A) was also formed together with *N*-methylindanthrone by heating 1-chloro-2-methylaminoanthraquinone with 2-aminoanthraquinone in the presence of copper or copper salts.

Hydrolysis of (A) afforded (B) and ultimately a mixture of 2-aminoanthraquinone and 2-formamidoanthraquinone. (B) was identical with the product obtained by condensing 2-aminoanthraquinone with ethyl orthoformate. It was transformed into (A) when heated with copper or copper salts. (A) was also prepared by condensing 2-aminoanthraquinone with formaldehyde and heating the resulting bis-2-anthraquinonylaminomethane with nitrobenzene and copper, or a copper salt. The constitution of (A) is considered.

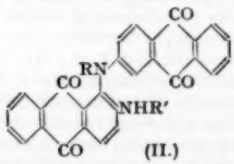
2-Dimethylaminoanthraquinone, when heated in nitrobenzene with an alkali and copper salt, afforded 2-methylaminoanthraquinone. 2-Methylaminoanthraquinone yielded (A) and formaldehyde. 2-*N*-Methylanilinoanthraquinone yielded formaldehyde and a product which gave the reactions of 2-anilinoanthraquinone. 2-Ethylaminoanthraquinone was similarly dealkylated. The condensation of 1-chloroanthraquinone and 2-methylaminoanthraquinone yielded 1 : 2′-dianthraquinonylamine and formaldehyde. 1-Methylaminoanthraquinone gave formaldehyde, 1-aminoanthraquinone, and 1-formamidoanthraquinone. Heated with 2-chloroanthraquinone, 1-methylaminoanthraquinone yielded formaldehyde and a mixture of 1 : 2′-dianthraquinonylamine and its *N*-methyl derivative.

The mechanism of the reactions is discussed.

In Part I* the preparation of the *N*-methyl and *NN*-dimethyl derivatives of indanthrone (I; R = R′ = H) was described. They were obtained by cyclising 2-amino- (II; R = Me, R′ = H) and 2-methylamino-1 : 2′-dianthraquinonyl-*N*-methylamine (II; R = R′ = Me) respectively; both were also prepared by the methylation of indanthrone. They had the



(I.)



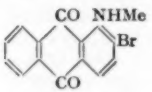
(II.)

expected properties, in particular, the dimethyl derivative dissolved in pyridine with a blue colour, which was not affected by the addition of methanolic potassium hydroxide, whilst the monomethyl derivative gave a blue solution which alkali rendered green. In G.P. 158,287 it is claimed that the dimethyl derivative results when 2-bromo-1-methylaminoanthraquinone is heated with sodium acetate and cupric chloride in nitrobenzene; it cannot be the only product of this reaction, however, because the product readily gives a green colour with methanolic potassium hydroxide in pyridine. In the present investigation the procedure

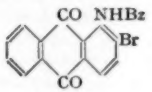
* Part I, preceding paper.

of G.P. 158,287 was repeated with a sample of 2-bromo-1-methylaminoanthraquinone (III) which was entirely free from the 1-amino-quinone. The purity was established by converting a portion into the *N*-benzoyl derivative, which gave a yellow solution in pyridine entirely unaltered by methanolic potassium hydroxide; in similar circumstances 1-benzamido-2-bromoanthraquinone (IV) afforded a deep red solution. The self-condensation of pure (III) yielded a blue colouring matter which again exhibited a green alkali colour reaction; during the condensation under a variety of conditions formaldehyde was liberated. The same result was obtained when copper bronze, cuprous chloride, and cupric acetate were used instead of cupric chloride. With cuprous chloride the yield of colouring matter increased slowly during 5 hours; with cupric acetate it reached a maximum at an earlier stage. The yield of formaldehyde increased throughout the reaction in all cases; in one experiment 61% of the methyl groups were eliminated as formaldehyde. It was then observed that both 2-bromo-1-methylaminoanthraquinone and *NN*-dimethylindanthrone are readily demethylated by heating them with copper salts.

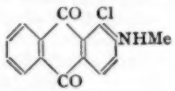
The crude colouring matter obtained by heating 2-bromo-1-methylaminoanthraquinone with cuprous chloride was mainly *N*-monomethylindanthrone; small quantities of indanthrone and, probably, dimethylindanthrone were separated by reduction and chromatography (see Experimental). *N*-Methylindanthrone recovered from the column was identical with the



(III.)



(IV.)



(V.)

product obtained by cyclising 2-amino-1 : 2′-dianthraquinonyl-*N*-methylamine (Part I) (cf. Fig. 1). The presence of indanthrone was confirmed by means of the reaction with a solution of nitric acid in sulphuric acid which yielded the yellow indanthroneazine.

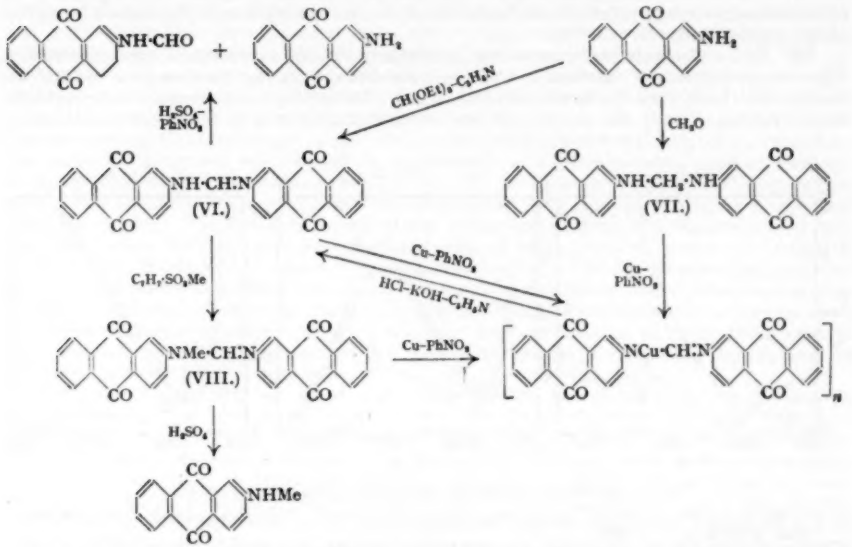
It has been stated (G.P. 234,294) that heating an equimolecular mixture of 1-amino-2-bromoanthraquinone and 2-bromo-1-methylaminoanthraquinone in nitrobenzene in the presence of cupric chloride and an alkali yields *N*-methylindanthrone. In the present experiments this procedure afforded also some indanthrone, 11% of the methyl groups being lost as formaldehyde after two hours.

1-Chloro-2-methylaminoanthraquinone (V) with copper sulphate and potassium acetate in nitrobenzene yielded both 2-methylamino- and 2-amino-anthraquinone, demethylation and dehalogenation having occurred. In a similar experiment with cuprous chloride all of the chlorine initially present appeared in the product as potassium chloride. There was no formation of indanthrone or a derivative of this in either instance. Maki and Mine (*J. Soc. Chem. Ind. Japan*, 1944, **47**, 522) similarly have been unable to prepare indanthrone by the self-condensation of 2-amino-1-chloroanthraquinone. In the second experiment the product contained a red crystalline compound, later identified as the cuprous derivative of *NN′*-di-2-anthraquinonylformamidine (VI); this contained all the copper present initially. The cuprous derivative of (VI) was also formed when *o*-dichlorobenzene was used in the place of nitrobenzene, and cupric acetate instead of cuprous chloride.

There was no reaction between 1-chloro-2-methylaminoanthraquinone and 2-amino-anthraquinone in the absence of copper salts. When cuprous chloride and potassium acetate were added, *N*-methylindanthrone was formed in small amount, but the main product was again the cuprous derivative of (VI); there was no indication of the presence of 2-methylamino-1 : 2′-dianthraquinonylamine.

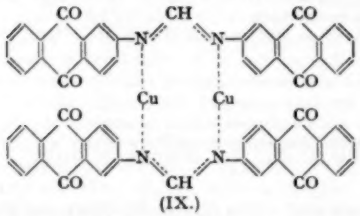
The constitution of the copper derivative of *NN′*-di-2-anthraquinonylformamidine (VI) follows from the following considerations. Analysis gives the composition $C_{29}H_{15}O_4N_2Cu$. Heating it with concentrated hydrochloric acid yields cuprous chloride, *NN′*-di-2-anthraquinonylformamidine. and 2-aminoanthraquinone. Heating it with pyridine and methanol containing potassium hydroxide also yielded the formamidine. *NN′*-Di-2-anthraquinonylformamidine, heated with acetic anhydride, yields 2-acetamidoanthraquinone; benzoyl chloride affords 2-benzamidoanthraquinone; hydrolysis with concentrated sulphuric acid gives 2-amino-anthraquinone; heating it with nitrobenzene containing a few drops of sulphuric acid yields 2-formamidoanthraquinone, identical with the product obtained by heating 2-aminoanthraquinone with formic acid. *NN′*-Di-2-anthraquinonylformamidine was synthesised by heating 2-aminoanthraquinone with ethyl orthoformate, following G.P. 248,656, and the cuprous derivative by combining 2-aminoanthraquinone with formaldehyde and oxidising the resulting

di-2-anthraquinonylaminomethane (VII) with copper bronze and nitrobenzene. The identities of the various formamidine preparations are confirmed by absorption spectra (Fig. 2).

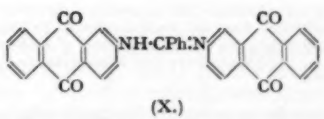


The same copper derivative was formed from (VI) whether copper was employed as copper bronze, cuprous chloride, or cupric acetate. Heating 1 mol. of cupric acetate with 2 mols. of (VI) yielded the same cuprous derivative, one half of the *NN'*-di-2-anthraquinonylformamidine employed remaining unchanged.

The copper derivative showed no tendency to combine with aniline, pyridine, ethylenediamine, or ammonia. It was only very slightly soluble in organic solvents and was hydrolysed by acids only with difficulty.



(IX.)



(X.)

In its stability and colour the copper derivative differed considerably from the cupric derivatives of acetylacetone (Morgan, Drew, and Porter, *Ber.*, 1925, **58**, 333), salicylaldoxime (Cox and Webster, *J.*, 1935, 731) salicylaldehyde (Tyson and Adams, *J. Amer. Chem. Soc.*, 1940, **62**, 1228), and salicylaldimine (Hunter and Marriott, *J.*, 1937, 2000). Copper phthalocyanine (Linstead *et al.*, *J.*, 1934, 1016), whilst more stable, has the typical colour of a cupric derivative. In colour, the red copper *NN'*-di-2-anthraquinonylformamidine derivative approaches more closely the violet-pink cuprous derivative of acetylacetone (Emmert and Gsottschneider, *Ber.*, 1936, **69**, 1319) and the brown cupric derivatives of *o*-hydroxyazobenzene (Hunter, *J.*, 1935, 1598) and 2 : 2'-dihydroxyazobenzene (Pfeiffer, Hesse, Pfitzner, Scholl, and Thielert, *J. pr. Chem.*, 1937, **149**, 235). Its chemical inertness indicates a high degree of covalency between copper and nitrogen (cf. Sherman and Randles, *J.*, 1941, 802; *Chem. Reviews*, 1932, **2**, 153) and a molecular constitution such as (IX) appears probable.

By contrast, the potassium derivative of (VI) was a typical salt soluble in pyridine with

a blue colour, stable towards dilution with alcohol but hydrolysed by water. *NN'*-Di-2-anthraquinonylformamidine was readily methylated to an orange monomethyl derivative (VIII), hydrolysed by sulphuric acid to 2-methylaminoanthraquinone. Heating (VIII) in nitrobenzene with copper bronze and potassium carbonate caused demethylation and formation of the cuprous derivative of (VI).

NN'-Di-2-anthraquinonylbenzamidine (X) similarly afforded a crystalline cuprous derivative. This was dark green by reflected, but red by transmitted light (for its absorption see Fig. 2). It was more basic than the formamidine analogue. Its sulphate was comparatively stable to water; correspondingly, the cuprous salt was less stable than that of the formamidine derivative;

FIG. 1. FIG. 2. FIG. 3.

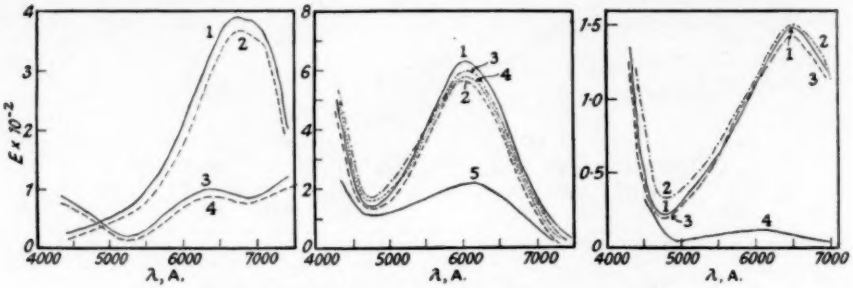


FIG. 1.—*N-Methylindanthrone and its potassium salt in pyridine.*

1, *N-Methylindanthrone obtained by the ring closure of 2-amino-1 : 2'-dianthraquinonyl-N-methylamine : Max. at* 6700 Å. (*E* = 390).
2, *Product obtained by the self-condensation of 2-bromo-1-methylaminoanthraquinone.*
3, *Potassium salt of the compound recorded in* (1), *formed by addition of methanolic potassium hydroxide to the pyridine solution : Min. at* 5250 Å. (*E* = 19), *max. at* 6350 Å. (*E* = 96), *min. at* 6900 Å. (*E* = 84).
4, *Potassium salt of the compound recorded in* (2).

FIG. 2.—*The potassium salts of dianthraquinonylamidines in pyridine.*

1, *NN'-Di-2-anthraquinonylformamidine : Min. at* 4800 Å. (*E* = 145), *max. at* 6050 Å. (*E* = 630).
2, *The same product* (*obtained from 2-methylaminoanthraquinone*).
3, *The same product* (*obtained from 2-dimethylaminoanthraquinone*).
4, *The same product* (*obtained from di-2-anthraquinonylaminomethane*).
5, *NN'-Di-2-anthraquinonylbenzamidine : Min. at* 4750 Å. (*E* = 120), *max. at* 6150 Å. (*E* = 210).

FIG. 3.—*1 : 2'-Dianthraquinonylamines in concentrated sulphuric acid.*

1, *1 : 2'-Dianthraquinonylamine : Min. at* 4800 Å. (*E* = 23), *max. at* 6500 Å. (*E* = 148).
2, *Product from the condensation of 2-chloroanthraquinone and 1-methylaminoanthraquinone.*
3, *Product from the condensation of 1-chloroanthraquinone and 2-methylaminoanthraquinone.*
4, *1 : 2'-Dianthraquinonyl-N-methylamine : Min. at* 5000 Å. (*E* = 5), *max. at* 6100 Å. (*E* = 11).

it was decomposed by heating it with pyridine or acetic acid. The simpler diarylformamidines appear to be basic compounds forming stable hydrochlorides.

Although condensation of aminoanthraquinones with halogenoanthraquinones in the presence of copper salts is a well-established method of preparing the dianthraquinonylamines, the occurrence of dealkylation appears not to have been observed. An investigation of the behaviour of simple alkylaminoanthraquinones towards copper and its salts gave the following results.

2-Methylaminoanthraquinone with potassium acetate and copper bronze in nitrobenzene readily yielded the copper derivative of (VI) and formaldehyde. The amount of the copper derivative increased with the time of heating. It was greatest when the copper catalyst used was cupric acetate, less when it was copper bronze and least, cuprous chloride; this was also the order of efficiency of the three catalysts for the production of formaldehyde from 2-dimethylaminoanthraquinone. The yield of the copper derivative of (VI) was smaller when *o*-dichlorobenzene or naphthalene replaced nitrobenzene as reaction medium; it was nil when the medium

was aniline, dimethylaniline, quinoline, or amyl alcohol. The addition of 5% of aniline to nitrobenzene greatly reduced the yield of the copper derivative.

2-Ethylaminoanthraquinone with copper bronze and potassium carbonate in nitrobenzene similarly yielded 2-aminoanthraquinone; 2-*N*-methylanilinoanthraquinone gave formaldehyde and a product which gave the deep green alkali colour reaction of 2-anilinoanthraquinone. 1-Methylaminoanthraquinone yielded formaldehyde, 1-aminoanthraquinone, and also 1-formamidoanthraquinone; in the presence of 2-chloroanthraquinone formaldehyde was again liberated and both 1 : 2′-dianthraquinonylamine and its *N*-methyl derivative were formed. (For the absorptions of products of these and similar reactions see Fig. 3.) Alkali colour reactions indicated the production of *NN*′-di-1-anthraquinonylformamidine in the last reaction; the product decomposed when heated in nitrobenzene or trichlorobenzene, yielding 1-aminoanthraquinone and 1-formamidoanthraquinone. An attempt to prepare *NN*′-di-1-anthraquinonylformamidine by heating 1-aminoanthraquinone with ethyl orthoformate in pyridine was unsuccessful. The formamidine containing *N*-1-anthraquinonyl substituents is evidently less stable than the isomeric compound containing 2-anthraquinonyl groups, a conclusion supported by the fact that, whilst the cuprous derivative of *NN*′-di-2-anthraquinonylformamidine is formed abundantly when 2-methylaminoanthraquinone is heated with nitrobenzene, potassium carbonate, and copper acetate, no corresponding copper derivative is formed when 1-methylaminoanthraquinone is similarly treated. Another instance of ready demethylation was encountered in the formation of *NN*′-di-2-anthraquinonylformamidine by heating its *N*-methyl derivative with copper salts.

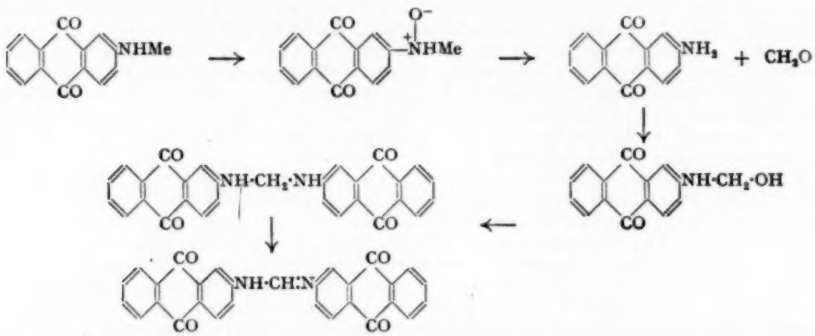
Particularly interesting in the present connection are the properties of *NN*-dimethylindanthrone. It has been shown (Part I) that *NN*-dimethylindanthrone yields *N*-methylindanthrone when it is added to concentrated nitric acid. A similar demethylation occurs when *NN*-dimethylindanthrone is heated in nitrobenzene with potassium carbonate and cupric acetate: formaldehyde is liberated in amount equivalent to 5% of the methyl groups after 5 hours. There is no demethylation when copper bronze is substituted for cupric acetate. An interesting fact, confirmed on several occasions, is that demethylation occurs when *NN*-dimethylindanthrone is heated in *o*-dichlorobenzene, and especially in nitrobenzene, in the presence of alumina. The products are *N*-methylindanthrone and indanthrone, the latter being strongly adsorbed on the alumina. Adsorption must increase the possibility of a reaction, and the greater adsorption of indanthrone must contribute to the result, even if demethylation is not determined by the adsorption factor.

The part played by adsorption in the demethylation process probably gains in importance by the fact that the molecule of indanthrone is planar. In contrast, in the *N*-methyl derivatives, the planes occupied by the component anthraquinone nuclei do not coincide, and the large angle of intersection is bisected by a third plane which carries the methyl groups.

The demethylation of amines in processes involving oxidation has been observed on numerous occasions. Hess, Merck, and Uibrig (*Ber.*, 1915, **48**, 1890) found that aldehydic and ketonic derivatives of 1-methylpyrollidine and 1-methylpiperidine were readily demethylated as a result of intramolecular oxidation–reduction, formaldehyde being liberated. Fischer and Fischer (*Ber.*, 1878, **11**, 1081) obtained formaldehyde on oxidation of malachite-green with manganese dioxide and sulphuric acid. Oxidised with osmium tetroxide and hydrogen peroxide, *p*-dimethylaminoazobenzene yielded both *p*-amino- and *p*-methylamino-azobenzene (Anderson, *Nature*, 1949, **163**, 444). Carter, Moulds, and Riley (*J.*, 1937, 1305) found that dimethylaniline heated with graphitic oxide afforded 4 : 4′-tetramethyldiaminodiphenylmethane; the same product had been obtained by the electrochemical oxidation of dimethylaniline (Fichter and Rothenberger, *Helv. Chim. Acta*, 1922, **5**, 166). A comprehensive survey of the oxidative demethylation of *N*-methyl compounds *in vivo* has been made by Challenger (*Chem. and Ind.*, 1942, **20**, 398).

While the production of formaldehyde or compounds derived from it is a well-established occurrence in the oxidation of methylated amines, the mode of its formation is less certain. Dehydrogenation of >CH·NH– to >C:N–, which occurs in the oxidation of α-amino- to α-keto-acids, could also explain the oxidation of tertiary amines in acid solution ($CH_3 \cdot NR_2 \xrightarrow{H^+} CH_2 \cdot NHR_2^+ \xrightarrow{-2H} CH_2{:}NR_2^+$). Experiment shows, however, that the demethylation of methylaminoanthraquinones and dianthraquinonyl-*N*-methylamines by copper salts is favoured by the presence of alkalis. An alternative view is that the liberation of formaldehyde is preceded by hydroxylation of the methyl group. This hypothesis has been adopted by Kruger and Oberlies (*Ber.*, 1941, **74**, 663) to account for the oxidation of dimethylaniline, and also by

Clarkson, Holden, and Malkin (*J.*, 1950, 1561) who showed that the oxidation of 2 : 4-dinitro-*NN*-dimethylaniline yielded formaldehyde, formic acid, and 2 : 4-dinitro-*N*-methylaniline. The production of a hydroxymethylamine at some stage in the total oxidation of 2-methylaminoanthraquinone appears to be necessary because the cuprous salt of *NN'*-di-2-anthraquinonylformamidine is a major product of the reaction and its formation is difficult to explain except by the interaction of 2-hydroxymethylaminoanthraquinone with 2-aminoanthraquinone followed by oxidation. It was shown that the yield of the cuprous derivative could be doubled by adding an equimolar amount of 2-aminoanthraquinone to the 2-methylaminoanthraquinone employed, and also that heating a mixture of 2-formamidoanthraquinone and 2-aminoanthraquinone did not yield *NN'*-di-2-anthraquinonylformamidine. All the results can be explained equally well, however, by the initial formation of an amine oxide, which decomposes to yield formaldehyde and 2-aminoanthraquinone.



The de-ethylation of 2-ethylaminoanthraquinone did not yield a formamidine derivative, nor did the reaction occur so readily as the demethylations. This accords with the greater stability of 5-ethylphenazinium ethyl sulphate in comparison with the *N*-methyl analogue (McIlwain, *J.*, 1937, 1705). The same relationship has been observed biologically in derivatives of glycine (Abbot and Lewis, *J. Biol. Chem.*, 1941, **137**, 535).

Experimental.

Condensation of 1-*Chloroanthraquinone and* 2-*Methylaminoanthraquinone.*—1-Chloroanthraquinone (4·8 g.), 2-methylaminoanthraquinone (4·7 g.), dry potassium acetate (3·0 g.), and copper bronze (0·4 g.) were heated under reflux with nitrobenzene (40 c.c.) for 18 hours. The solution was filtered hot, and the residue (2·6 g.) washed with alcohol and then water. Reddish-brown prisms (0·55 g.), which crystallised from the nitrobenzene filtrate, did not melt below 300° (Found: C, 77·9; H, 3·5; N, 3·3. Calc. for $C_{28}H_{18}O_4N$: C, 78·3; H, 3·5; N, 3·3%); they were identified as 1 : 2′-dianthraquinonylamine by the green colour and absorption spectrum of a solution in concentrated sulphuric acid (Fig. 2), and by the green colour developed when methanolic potassium hydroxide was added to an orange solution of the product in pyridine. The residue (2·6 g.) was extracted by acetic acid or concentrated aqueous ammonia and ammonium chloride until copper no longer dissolved; the residual *copper* derivative (2·3 g.) consisted of hair-like red needles (A) (Found: C, 67·4; H, 3·0; N, 5·5; Cu, 12·7, 12·3, 11·8. $C_{29}H_{18}O_4N_2Cu$ requires C, 67·1; H, 2·9; N, 5·4; Cu, 12·3%).

Further experiments showed that (A) was derived from 2-methylaminoanthraquinone.

Conversion of 2-*Methylaminoanthraquinone into the Cuprous Derivative* (A) *of* NN'-*Di*-2-*anthraquinonylformamidine.*—The variation in the yield of (A) from 2-methylaminoanthraquinone with the experimental conditions is shown in the following Tables. For work reported in the second Table the time of heating was 24 hours and the added alkali potassium carbonate.

2-Methylamine-anthraquinone (g.).	Alkali (g.).	Copper bronze (g.).	Nitro-benzene (c.c.).	Time (hrs.).	Yield of A (g.).
10	6 (KOAc)	0·8	80	16	2·7
5	absent	absent	40	16	0
5	absent	0·4	40	16	0
0	3 (KOAc)	0·4	40	16	0
10	6 (KOAc)	2·0	80	5	6·4
5	3 (K_2CO_3)	1·0	40	5	2·0

Solvent.	Copper or copper derivative.	Yield (%) of A, calc. on 2-methylaminoanthraquinone.
Nitrobenzene	Copper bronze	75 *
	Cuprous chloride	16
	Cupric acetate	84
o-Dichlorobenzene	Copper bronze	0
	Cuprous chloride	2
	Cupric acetate	17
Naphthalene	Copper bronze	0
	Cupric acetate	10

* In a parallel experiment, in which an equimolecular amount of 2-aminoanthraquinone was added to the reactants, the yield of A was increased to 134%.

The compound A was not formed when the solvent was aniline, dimethylaniline, quinoline, or amyl alcohol, whether copper bronze or cupric acetate was used. In the nitrobenzene–copper bronze experiment the yield was reduced to 8% when 5% of aniline was added to the reactants. In the nitrobenzene–cuprous chloride experiment, aniline was found in the product.

Product A was insoluble in the available organic solvents; it was recovered unaltered after being heated with acetic anhydride. It gave a blue solution in pyridine containing a few drops of methanolic potassium hydroxide. Identical copper derivatives were formed when the copper bronze was replaced by cuprous chloride (Found: Cu, 12·2%) and cupric acetate (Found: Cu, 13·0%).

Hydrolysis. (*a*) Product A (1·0 g.) was heated with concentrated hydrochloric acid (100 c.c.) at the b. p.; after 30 minutes the solution had become yellow and a grey precipitate had separated. The suspension was filtered hot and the residue washed with water and then dilute aqueous ammonia. During the ammonia washing it became brown; the dried residue was an orange-brown powder (0·7 g.). Crystallisation from nitrobenzene gave NN′-*di*-2-*anthraquinonylformamidine* as small orange needles (B), m. p. 385—390° (Found: C, 76·0; H, 3·3; N, 6·3. $C_{29}H_{16}O_4N_2$ requires C, 76·3; H, 3·5; N, 6·1%).

The hydrochloric acid filtrate contained a soluble copper salt. Addition of ammonia gave an orange-brown precipitate (0·15 g.) of crude 2-aminoanthraquinone, m. p. 270°. Acetylation gave yellow prisms, m. p. 266—267°, not depressed on admixture with authentic 2-acetamidoanthraquinone.

(*b*) Product A (1·0 g.) was heated under reflux with pyridine (50 c.c.) and methanolic potassium hydroxide (3 c.c. of 30%). After 10 minutes' boiling the blue solution was filtered and the filtrate added to methyl alcohol (300 c.c.). The orange-brown precipitate (0·6 g.) which formed was filtered off and crystallised from nitrobenzene as orange needles, m. p. 380—390° (decomp.) (Found: C, 75·8; H, 3·4; N, 6·1%). Compound B dissolved in concentrated sulphuric acid with an orange-brown colour; on addition of water the solution became colourless. It dissolved in pyridine with a yellow colour; a deep blue colour developed on addition of methanolic potassium hydroxide, and this became violet and finally yellow on addition of methyl alcohol.

Conversion of B *into* A.—The copper derivative was formed when B was heated with copper or one of its salts under a variety of conditions as shown in the annexed Table. The copper derivative obtained by heating B with cupric acetate in nitrobenzene was analysed (Found: C, 66·6; H, 2·8; N, 5·7; Cu, 12·5%).

Amount of B (g.).	Solvent.	Vol. (c.c.).	Copper or copper derivative.	Yield (g.).	Time (hrs.).	Conversion.
0·5	$PhNO_2$	30	Cu bronze	0·2	0·5	Complete
0·2	,,	20	Absent	—	2·0	None
0·5	,,	20	Cu powder	0·2	2·0	Complete, slow
0·2	,,	20	$CuAc_2$	0·5	0·5	Complete, 10 mins.
0·5	,,	50	CuCl	0·2	2·0	Incomplete
0·05	*o*-$C_6H_4Cl_2$	5	Cu bronze	0·25	24·0	Incomplete
0·05	,,	5	CuCl	0·2	24·0	Incomplete
0·02	,,	5	$CuAc_2$	0·02	4·0	Complete, rapid
0·5	C_5H_5N	100	CuCl–KOAc	0·3, 0·05	2·0	Amorphous product
0·1	,,	100	$CuAc_2$	0·2	1·0	—

Reactions of (B).—(a) *Acetylation.* A suspension of B (1·0 g.) in acetic anhydride (50 c.c.) was heated under reflux for 30 minutes. The solution was filtered from undissolved material (0·05 g.) and then mixed with an equal volume of water; a brown solid (0·5 g.), m. p. 255—260°, separated and, recrystallised from acetic acid, afforded yellow prisms, m. p. 266—267°, not depressed on admixture with authentic 2-acetamidoanthraquinone.

(b) *Benzoylation.* A suspension of B (1·0 g.) in benzoyl chloride (50 c.c.) was heated under reflux for 30 minutes. A clear, dark yellow solution resulted, and from this crystals, m. p. 210—235° (0·1 g.), separated on cooling. Addition of alcohol to the mother-liquor gave crystals, m. p. 230° (0·2 g.), and these separated from nitrobenzene in yellow needles, m. p. 233—234°, not depressed on admixture with 2-benzamidoanthraquinone.

(c) *Hydrolysis.* (i) A solution containing B (1·0 g.) in concentrated sulphuric acid (200 c.c.) was prepared at room temperature, and then kept for 4 days. It was then added to water; a yellow precipitate (0·8 g.; m. p. 284—300°) formed. This was dissolved in benzene and chromatographed on alumina. Two zones formed. The less strongly adsorbed, orange zone was eluted by means of acetone, yielding 2-aminoanthraquinone, further characterised by the acetyl and benzoyl derivatives. (ii) To B (0·5 g.)

in boiling nitrobenzene (300 c.c.) a few drops of concentrated sulphuric acid in nitrobenzene were added, the heating was continued for 5 minutes, and the whole then concentrated to half-volume by distillation. Brownish-yellow crystals, m. p. 285—290°, which separated, recrystallised from *o*-dichlorobenzene as star-shaped clusters of pale yellow, fine needles, m. p. 291—292° (Found : C, 71·8; H, 3·7; N, 5·7. $C_{15}H_9O_3N$ requires C, 71·7; H, 3·6; N, 5·6%). This product was identical with *2-formamidoanthraquinone* prepared in the following way. 2-Aminoanthraquinone (5·0 g.) and 98% formic acid (15 c.c.) were heated for 5 hours at 170°. The product (5·25 g.), crystallised twice from nitrobenzene, yielded 4·1 g. of 2-formamidoanthraquinone, m. p. 291—292° (Found : C, 71·7; H, 3·7; N, 5·3%).

(d) *Reduction.* To sodium hydroxide (1 g.) and sodium dithionite (0·3 g.) in water (50 c.c.) was added 0·3 g. of (B). On being warmed to 70°, B dissolved with a deep brownish-red colour; the solution was boiled for 10 minutes, then filtered hot. The filtrate, aerated, gave 0·2 g. of orange material, m. p. 270—280°. This was sublimed at 280°/0·1 mm. and the sublimate (m. p. 290—300°) acetylated. The product had m. p. 266°, not depressed on admixture with 2-acetamidoanthraquinone.

Bis-2-anthraquinonylaminomethane.—2-Aminoanthraquinone (5·0 g.) was made into a paste with 40% formaldehyde (25 c.c.), then heated at 100° for 12 hours. The product (4·5 g.; m. p. 304°) was collected, washed with water, and extracted by acetic acid. A sparingly soluble orange residue (1·6 g.) was crystallised from 600 c.c. of nitrobenzene (charcoal), yielding 0·8 g. of *bis-2-anthraquinonylaminomethane* as orange, short, prismatic needles, m. p. 332—334° (decomp.) (Found : C, 75·6; H, 4·2; N, 6·3. $C_{29}H_{18}O_4N_2$ requires C, 76·0; H, 3·9; N, 6·1%). This was probably the main constituent of the substance, m. p. 325—335° (not analysed), obtained according to G.P. 287,907 by condensing formaldehyde with 2-aminoanthraquinone in the presence of mineral acids. The product, m. p. 332—334°, was not affected by boiling concentrated hydrochloric acid or acetic anhydride, nor was formaldehyde produced when the product was heated with sulphuric acid in a current of air. It was unaffected by long exposure to light.

Under other conditions the condensation took a different course (cf. U.S.P. 2,091,235).

A solution containing 2-aminoanthraquinone (5 g.) in concentrated sulphuric acid (100 c.c.) was cooled to 0° and then added at 0° to a stirred solution containing paraformaldehyde (6 g.) in concentrated sulphuric acid (100 c.c.). After 2 hours at 0°, and then at the room temperature for 12 hours, the solution was added to water. The red precipitate was collected, washed with dilute aqueous ammonia, and the dried, insoluble portion (6·6 g.) crystallised from nitrobenzene. The red needles (4·5 g.; m. p. 220—230°) so obtained were chromatographed on alumina from a solution in benzene (0·5 g. in 300 c.c.). Two main zones resulted. The upper zone yielded 0·03 g. of orange needles, m. p. 306°, which with hot acetic anhydride gave 2-acetamidoanthraquinone, m. p. 265—266°. The lower red zone, eluted by methanol, afforded 0·25 g. of reddish-orange needles, m. p. 232°, alone or mixed with 2-methylaminoanthraquinone.

NN'-*Di-2-anthraquinonylformamidine.*—(*a*) The compound, m. p. 332—334° (0·8 g.), was heated under reflux with copper bronze (0·4 g.) and potassium carbonate (0·4 g.) in nitrobenzene (40 c.c.) for an hour. Red needles (1·1 g.) which separated were filtered off and heated under reflux with concentrated hydrochloric acid (100 c.c.). The undissolved material crystallised from nitrobenzene in orange-yellow needles (Found : C, 75·8; H, 3·8; N, 6·4. Calc. for $C_{29}H_{16}O_4N_2$: C, 76·3; H, 3·5; N, 6·1%). This product was identical with (B), prepared as above. In pyridine it formed a solution which became blue on addition of methanolic potassium hydroxide. The absorption spectrum of the blue solution was identical with that of B (Fig. 2).

(*b*) The same compound B was also prepared by condensing 2-aminoanthraquinone with ethyl orthoformate, essentially by the method of G.P. 248,656. It crystallised from nitrobenzene in fine orange needles, m. p. 385—390° (decomp.) (Found : C, 76·2; H, 3·4; N, 6·4%), and gave in pyridine a yellow colour which became deep blue on addition of methanolic potassium hydroxide. Its solubility in hot nitrobenzene was approx. 0·16%.

Copper derivative. Heated in nitrobenzene with copper acetate the dianthraquinonylformamidine yielded a cuprous derivative, in the form of red, hair-like needles, identical with (A) (below).

(*c*) Heating 2-aminoanthraquinone (2·0 g.), paraformaldehyde (0·5 g.), potassium carbonate (1·0 g.), and copper bronze (0·5 g.) in nitrobenzene (40 c.c.) gave red needles (A) in 10 minutes. After 1·5 hours, the suspension was filtered while hot, and the residue (2·4 g.) extracted by acetic acid. The yield of residual cuprous derivative was 2·0 g. (86% calc. on the 2-aminoanthraquinone used). When potassium carbonate was omitted the reaction progressed more slowly; after 6 hours the yield of cuprous derivative was only 11%.

NN'-*Di-2-anthraquinonyl-N-methylformamidine.*—*NN'*-Di-2-anthraquinonylformamidine (1·0 g), methyl toluene-*p*-sulphonate (1·0 g.), and potassium carbonate (0·75 g.) were heated under reflux in trichlorobenzene (80 c.c.) for 5 hours; the formamidine derivative dissolved in 2 hours. On cooling, the filtered solution gave orange needles of the *methyl* derivative (0·65 g.), m. p. 316—317° (Found : C, 76·1; H, 3·6; N, 6·1. $C_{30}H_{18}O_4N_2$ requires C, 76·6; H, 3·8; N, 6·0%). It dissolved in pyridine with a yellow colour, unchanged by methyl alcoholic potassium hydroxide.

An identical compound, m. p. 316—317°, not depressed when mixed with the above *N*-methyl derivative, was obtained by treating (B) with methyl toluene-*p*-sulphonate and potassium carbonate under the conditions above described.

Heating the copper derivative (A) (3·0 g.) with methyl iodide (10 c.c.) at 150—160° for 10 hours gave only the copper-free *NN'*-di-2-anthraquinonylformamidine, m. p. >360°, characterised by the blue colour given on addition of methyl alcoholic potassium hydroxide to its solution in pyridine.

Hydrolysis. The above methyl derivative (0·1 g.) was heated in concentrated sulphuric acid (10 c.c.) to 100°, and allowed to cool. After being kept overnight the brown solution was added to water. A white precipitate formed, and this became orange when the acid was neutralised by ammonia.

The dried product (0·09 g.), m. p. 215—259°, was dissolved in benzene and chromatographed on alumina; two zones resulted. The upper zone, eluted with acetone, afforded orange needles, m. p. 290—300°. The lower, reddish-violet zone, eluted with acetone, yielded red, prismatic needles, m. p. 230°, alone or mixed with 2-methylaminoanthraquinone.

Demethylation of 2-Methylaminoanthraquinone.—(*a*) 2-Methylaminoanthraquinone (10·0 g.), dry potassium carbonate (6·0 g.), copper bronze (2·0 g.), and nitrobenzene (80 c.c.) were heated under reflux in a current of air which had been passed through an aqueous solution of 2 : 4-dinitrophenylhydrazine hydrochloride and then dried by calcium chloride. The volatile products of the reaction were passed through a vertical condenser, then through a trap, and finally through a solution of 2 : 4-dinitrophenylhydrazine in 2N-hydrochloric acid. Yellow needles of formaldehyde 2 : 4-dinitrophenylhydrazone, m. p. 165—166°, separated. After 5 hours the mitrobenzene suspension was distilled in steam. The residue (5·2 g.), m. p. 228°, was chromatographed in benzene on alumina. Two bands formed, an upper zone of strongly adsorbed black material, and a lower zone, which afforded red needles of 2-methylaminoanthraquinone. In this experiment the yield of (A) was 4·0 g.

(*b*) In a similar experiment in which 3·4 g. of cuprous chloride were used instead of copper bronze and the reaction time was 24 hours, the yield of (A) was 1·76 g. From the mother-liquor 2-methylaminoanthraquinone (4·0 g.) separated. After removal of this derivative, the nitrobenzene solution was washed with 10% hydrochloric acid. The acid extract was cooled to 0°, sodium nitrite (0·5 g.) was added, and the yellow solution added to one of β-naphthol (1 g.) in aqueous sodium hydroxide. The reddish-brown precipitate was collected, washed with aqueous sodium hydroxide, dried, and chromatographed in toluene on alumina. The main orange zone, eluted by methyl alcohol, afforded 1-phenylazo-2-naphthol, m. p. 130°, not depressed on admixture with an authentic sample.

Demethylation of 2-Dimethylaminoanthraquinone.—2-Dimethylaminoanthraquinone (2·5 g.), potassium carbonate (1·5 g.), and copper bronze (0·5 g.) were heated under reflux in nitrobenzene (20 c.c.) for 24 hours. The yield of (A) was 0·39 g. The nitrobenzene solution was distilled in steam, leaving a dark brown residue (2·2 g.). A portion (0·5 g.) of this was chromatographed in benzene (200 c.c.) on alumina; three zones formed. The most strongly adsorbed was black. Two red zones were eluted by acetone; the more strongly adsorbed of these yielded 0·05 g. of 2-methylaminoanthraquinone, m. p. 231°, not depressed on admixture with the authentic compound. The other yielded 0·35 g. of unchanged 2-dimethylaminoanthraquinone, m. p. 186°.

The 2-dimethylaminoanthraquinone used in this experiment was chromatographed before use and shown to be free from 2-methylaminoanthraquinone. The use of 0·85 g. of cuprous chloride instead of the copper bronze led to the formation of 0·31 g. of (A); when 1·5 g. of cupric acetate were used, the yield of (A) was 0·49 g.

Dealkylation of 2-Ethylaminoanthraquinone.—2-Ethylaminoanthraquinone (2·0 g.), potassium carbonate (1·5 g.), copper bronze (0·5 g.), and nitrobenzene (25 c.c.) were heated under reflux for 24 hours. When the mixture was then set aside, a dark product separated from the medium; this was collected and chromatographed in benzene on alumina. The main zone, extracted with ethyl alcohol, afforded 0·15 g. of unchanged 2-ethylaminoanthraquinone. A more strongly adsorbed orange zone gave, with acetone, 0·02 g. of needles, m. p. 302°. This product, acetylated, yielded 2-acetamidoanthraquinone, m. p. 266—267°, not depressed on admixture with an authentic sample.

Demethylation of NN'-Di-2-anthraquinonyl-N-methylformamidine.—A solution of the above formamidine (0·05 g.) in nitrobenzene (5 c.c.) was heated under reflux for 3 hours with potassium carbonate (0·10 g.) and copper bronze (0·05 g.). The hot solution was filtered; the residue contained the characteristic red needles of (A), the identity of which was further confirmed by the deep blue colour obtained on heating to boiling a suspension of the product in pyridine containing methanolic potassium hydroxide. In a similar experiment in which the potassium carbonate was omitted the original formamidine (0·04 g.) was recovered unchanged; there was no indication of the occurrence of demethylation.

NN'-Di-2-anthraquinonylbenzamidine.—This was prepared by the method of G.P. 248,656. Crystallised from *o*-dichlorobenzene it formed fine yellow prismatic needles, m. p. 327° (Found: C, 78·4; H, 3·9; N, 4·8. Calc. for $C_{35}H_{20}O_4N_2$: C, 78·9; H, 3·8; N, 5·3%). *NN'*-Di-2-anthraquinonylbenzamidine dissolved in concentrated sulphuric acid with a reddish-brown colour; on addition of water, the buff-coloured sulphate separated; on the further addition of aqueous ammonia the yellow free base was regenerated. It dissolved in hot pyridine with a yellow colour, changed by methyl alcoholic potassium hydroxide to a greenish-blue; addition of alcohol caused a change to violet and ultimately to yellow.

Hydrolysis. A solution containing the benzamidine (1·0 g.) dissolved in concentrated sulphuric acid (10 c.c.) was heated for a few minutes to 200°, then cooled, and added to water. The orange precipitate was collected and washed with dilute aqueous ammonia. Evaporation of the washings and acidification gave 0·01 g. of benzoic acid, m. p. 120°. The insoluble residue (0·8 g.) was heated under reflux with acetic anhydride. The yellow product which separated recrystallised from acetic acid as yellow prisms, m. p. 264—265° alone or mixed with 2-acetamidoanthraquinone.

Copper derivative. A solution of the benzamidine (0·5 g.) in nitrobenzene (20 c.c.) was heated under reflux for 6 hours with copper bronze (0·25 g.). The residue obtained on filtering the hot suspension was stirred for 24 hours with a mixture of concentrated aqueous ammonia and ammonium chloride. The residue was then free from copper bronze; it was collected (0·11 g.) and obtained in the form of dark, olive-green, prismatic needles, which appeared red by transmitted light (Found: C, 70·2; H, 3·3; N, 4·6; Cu, 10·9. $C_{35}H_{19}O_4N_2Cu$ requires C, 70·7; H, 3·2; N, 4·7; Cu, 10·7%). When finely divided the *copper* derivative appeared reddish-brown. It decomposed on being heated with either pyridine, or acetic acid, the free benzamidine passing into solution.

Demethylation of 2-N-Methylanilinoanthraquinone.—2-*N*-Methylanilinoanthraquinone (1·0 g.), potassium carbonate (0·5 g.), cupric acetate (0·5 g.), and nitrobenzene (40 c.c.) were heated under reflux

in a slow stream of air. The volatile products were passed through a solution of dimedone; formaldehyde was detected after an hour. After 10 hours, the suspension containing the dimedone precipitate was set aside for 12 hours and then filtered. The yield of condensation product was 0·023 g., equivalent to the demethylation of 2·5% of the 2-*N*-methylanilinoanthraquinone.

The nitrobenzene solution was distilled in steam; a residue (1·1 g) was chromatographed in benzene on alumina. A continuous orange zone formed. This was cut into three equal portions and from each of these the adsorbed colouring matter was eluted by acetone. That from the most strongly adsorbed section (0·1 g.; m. p. 170—215°) dissolved in pyridine with an orange colour, changed to deep green by methanolic potassium hydroxide. The two remaining sections yielded unchanged 2-*N*-methylanilinoanthraquinone, m. p. 163° (0·65 g.).

1 : 2′-Dianthraquinonyl-*N*-methylamine was recovered unaltered (0·45 g.; m. p. 285°) when 0·5 g. was heated for 30 hours with copper bronze (1·0 g.) and potassium carbonate (1·0 g.) in nitrobenzene (50 c.c.). Neither formaldehyde nor formate could be detected, and the absence of 1 : 2′-dianthraquinonylamine was shown by the negative response of the product in the pyridine–methanolic potassium hydroxide test. A similar result was obtained when cupric acetate was used instead of copper bronze.

Demethylation of 1-*Methylaminoanthraquinone.*—(*a*) A suspension containing 1-methylaminoanthraquinone (2·5 g.), cupric acetate (1·5 g.) and potassium carbonate (1·5 g.) in nitrobenzene (20 c.c.) was heated under reflux for 24 hours, then filtered hot. The residue gave a negative response in the pyridine–methanolic potassium hydroxide test. The filtrate was distilled in steam; the residue was chromatographed in benzene on alumina. In addition to a lower violet zone from which 1-methylaminoanthraquinone, m. p. 170°, was recovered, there was a more strongly adsorbed red zone which yielded 1-aminoanthraquinone, m. p. 252°, on extraction with acetone. There was no indication of the presence of 1-formamidoanthraquinone.

(*b*) 1-Methylaminoanthraquinone (5·0 g.), potassium carbonate (5·0 g.), and copper bronze (2·0 g.) were heated under reflux in nitrobenzene (50 c.c.) in a current of dry air for 8 hours. Formaldehyde was liberated almost immediately; it was collected in dimedone solution and in this way yielded 0·29 g. of the condensation product, equivalent to the demethylation of 5% of the 1-methylaminoanthraquinone employed. The nitrobenzene solution was filtered hot; there was a residue (3·1 g.) consisting mainly of copper bronze. The filtrate deposited a brown solid [C; 0·8 g.; m. p. 284° (decomp.)] on storage. Product C formed in pyridine a yellow solution which became green on addition of methanolic potassium hydroxide, and violet on the further addition of alcohol. It formed a brown solution in concentrated sulphuric; this became colourless on addition of water, and an orange-red precipitate formed on further dilution. There was no indication of the formation of a copper derivative when C was heated with cupric acetate in nitrobenzene. Crystallisation from nitrobenzene and then from acetic acid gave an orange-red product, m. p. 180—186°. Dissolved in toluene and chromatographed on alumina, the product yielded a main orange-yellow zone. The lowest third extracted by means of acetone yielded fine red needles, m. p. 252·5°, not depressed by 1-aminoanthraquinone. The top third yielded orange needles, m. p. 206—220°; these were dissolved in benzene and again chromatographed on alumina. A continuous zone resulted; the lower half yielded a further quantity of 1-aminoanthraquinone. The upper half yielded orange needles, m. p. 223—224°, not depressed on admixture with 1-formamidoanthraquinone. This product dissolved in pyridine with a yellow colour, changed to reddish-orange by methanolic potassium hydroxide.

1-Aminoanthraquinone and 1-formamidoanthraquinone were also obtained when trichlorobenzene was substituted for nitrobenzene in the recrystallisation of C.

1-*Formamidoanthraquinone.*—1-Aminoanthraquinone (5 g.) was made into a paste with 98% formic acid (15 c.c.) and heated at 170—180° for 6 hours. The *formyl* derivative (5·2 g.; m. p. 215°) crystallised from acetic acid as orange meedles, m. p. 222—223° (Found: C, 71·4; H, 3·7; N, 5·5. $C_{11}H_9O_2N$ requires C, 71·7; H, 3·6; N, 5·6%). Its yellow solution in pyridine becomes red when methyl-alcoholic potassium hydroxide is added.

There was no reaction when 1-aminoanthraquinone (2 mols.) was heated with ethyl orthoformate (1 mol.) in nitrobenzene. 1 Aminoanthraquinone (5 g.) with ethyl orthoformate (11 c.c.) in nitrobenzene (50 c.c.) at 140° (4 hours) yielded a product (3·1 g.) which crystallised from acetic acid in orange needles, m. p. 177—178°. Warmed with concentrated sulphuric acid at 100° for an hour, this compound yielded 1-aminoanthraquinone, m. p. 252°.

Condensation of 1-*Methylaminoanthraquinone and* 2-*Chloroanthraquinone.*—1-Methylaminoanthraquinone (4·7 g.), 2-chloroanthraquinone (4·8 g.), potassium acetate (5·0 g.), and cuprous chloride (0·5 g.) were heated under reflux in nitrobenzene (50 c.c.) for 40 hours, whilst a current of air was passed through the mixture and thence through a solution of dimedone. The formaldehyde–dimedone condensation product was observed after 16 hours; the final yield was 0·029 g. The nitrobenzene solution was filtered hot; on cooling, red prisms of 1 : 2′-dianthraquinonylamine (2·5 g.) separated. This product was characterised by its absorption spectrum in concentrated sulphuric acid (Fig. 3), the green colour obtained on addition of methanolic potassium hydroxide to its solution in pyridine, and by the *N*-benzoyl derivative, m. p. 272—273°, not depressed when mixed with authentic *N*-benzoyl-1 : 2′-dianthraquinonylamine. When kept for several days the nitrobenzene mother-liquor yielded 1·9 g. of red crystals, m. p. 265—275°. Recrystallisation from nitrobenzene gave a product, m. p. 280—281°, not depressed by an authentic sample of 1 : 2′-dianthraquinonyl-*N*-methylamine, m. p. 283—284°. The product dissolved in pyridine with an orange colour, unchanged by methanolic potassium hydroxide.

Condensation of 1-*Chloro*-2-*methylaminoanthraquinone with* 2-*Aminoanthraquinone.*—1 Chloro-2-methylaminoanthraquinone (2·7 g.), 2-aminoanthraquinone (2·25 g.), potassium acetate (1·5 g.), and cuprous chloride (0·2 g.) were heated under reflux in nitrobenzene (20 c.c.). After 3 hours the solution was greenish-blue. It was filtered whilst hot and the residue was washed with water. The residue

consisted of reddish-brown crystals (0·8 g.) (Found: N, 5·1; Cu, 11·8. Calc. for $C_{29}H_{15}O_4N_3Cu$: N, 5·1; Cu, 12·2%) of the cuprous derivative of *NN'*-di-2-anthraquinonylformamidine. It was entirely free from chlorine. The filtrate yielded on cooling a black, indefinitely crystalline product, m. p. 237° (1·7 g.). This was chromatographed in chlorobenzene on alumina; three main zones resulted. The most strongly adsorbed, blue zone, eluted by *o*-dichlorobenzene, gave well-defined blue needles (0·02 g.) which crystallised well from quinoline and showed the characteristic properties of *N*-methylindanthrone. Its solubility in *o*-dichlorobenzene at 20° was 0·0015 g./100 c.c. Under identical conditions the solubility of a specimen of methylindanthrone prepared by the cyclisation of 2-amino-1 : 2′-dianthraquinonyl-*N*-methylamine was 0·00076 g. The total solubility of a mixture of the two specimens was 0·0013 g.

2-*Bromo*-1-*methylaminoanthraquinone*.—This *quinone* was prepared by the method of G.P. 288,825. The crude dark violet-red product, m. p. 140—150°, was crystallised several times from acetic acid and obtained in the form of red, prismatic needles, m. p. 170—171° (Found: C, 57·4; H, 3·3; N, 4·5; Br, 25·2. $C_{15}H_{10}O_2NBr$ requires C, 57·0; H, 3·2; N, 4·4; Br, 25·3%).

2-*Bromo*-1-*N*-*methylbenzamidoanthraquinone*.—A mixture of 2-bromo-1-methylaminoanthraquinone (1·0 g.), benzoyl chloride (3 c.c.), pyridine (5 c.c.), and a drop of concentrated sulphuric acid was heated to boiling. The solution became yellow after 5 minutes. It was added to alcohol and the precipitate (0·85 g.; m. p. 172—173°) collected. Recrystallisation from acetic acid gave yellow plates of 2-*bromo*-1-*N*-*methylbenzamidoanthraquinone* (0·62 g.), m. p. 176—177° (Found: N, 3·6. $C_{22}H_{14}O_2NBr$ requires N, 3·3%).

Self-condensation of 2-*Bromo*-1-*methylaminoanthraquinone*.—In the experiments recorded in the annexed Table 2-bromo-1-methylaminoanthraquinone (R) was heated under reflux with copper bronze (Cu), cuprous chloride, or cupric acetate and either sodium acetate or potassium acetate in nitrobenzene. A slow current of dry air was drawn through the reactants and any formaldehyde produced was absorbed in a 0·2% dimedone solution. At the end of the experiment the nitrobenzene suspension was cooled and then filtered. The residue was washed with alcohol, then with distilled water, and extracted by ammonia and ammonium chloride to remove copper and its salts. The undissolved residue was blue and consisted mainly of *N*-methylindanthrone. The distilled aqueous extract was acidified with nitric acid, and bromide ion precipitated as silver bromide; when cuprous chloride was used as condensing agent it was assumed that the all the halogen would appear in the silver precipitate as silver chloride.

	Reactants.					Products and yields (%).		
Exp. no.	R (g.).	Cu or Cu salt (g.).	NaOAc/KOAc (g.).	$PhNO_2$ (c.c.).	Time (hrs.).	Blue product.	CH_2O.	AgBr.
1	5	CuCl (0·25)	KOAc (3·0)	50	1	20	0	36
2	,,	,,	,,	60	5	46	11	83
3	1	Cu (0·1)	NaOAc (0·5)	20	2	12	30	trace
4	2	$Cu(OAc)_2$ (0·2)	NaOAc (1·0)	40	1	7	24	2
5	,,	,,	,,	,,	2	6	48	trace
6	,,	,,	,,	,,	4	6	61	,,
7	*	CuCl (0·2)	KOAc (2·4)	50	2	64	11	64

* The reactants were 1-amino-2-bromo- (1·8 g.) and 2-bromo-1-methylamino-anthraquinone (1·9 g.).

The nitrobenzene mother-liquor of experiment 5 was distilled in steam, and the dark reddish-brown residue was chromatographed in benzene on alumina. Elution with benzene gave first red-violet needles of 2-bromo-1-methylaminoanthraquinone, and then fine orange needles of 1-amino-2-bromoanthraquinone, m. p. 177—178°, not depressed on admixture with an authentic sample.

The colouring matter obtained in experiment 1 approximated in composition and properties to *N*-methylindanthrone. It crystallised from quinoline in short, violet needles (Found: C, 76·0; H, 3·5; N, 5·8; NCH_3, 6·3. Calc. for $C_{29}H_{14}O_4N_2$: C, 76·3; H, 3·5; N, 6·1; NCH_3, 6·4%). It dissolved in concentrated sulphuric acid with a brown colour and with the same colour in alkaline dithionite.

(*a*) A solution containing 0·5 g. of the product in concentrated sulphuric acid (4 c.c.) was cooled to 0°, a suspension of sodium nitrate (0·4 g.) in concentrated sulphuric acid (2 c.c.) was added, and the mixture stirred for an hour. Glacial acetic acid (20 c.c.) was then added, the product kept for 16 hours, and then the brown precipitate was collected. After being washed with sodium carbonate solution it was dissolved in alkaline dithionite. Aeration of the filtered blue solution gave indanthrone. The product crystallised from quinoline in the violet-blue curved needles characteristic of indanthrone.

(*b*) The blue product (0·05 g.) was dissolved in hot *o*-dichlorobenzene (100 c.c.) and poured on a column of alumina, previously heated for several hours at 140—150°. Development with a 20% solution of quinoline in *o*-dichlorobenzene at 140—150° gave a lower band of *N*-methylindanthrone, and a strongly adsorbed band of indanthrone.

(*c*) The blue product was recovered unaltered after being heated under reflux with quinoline or *o*-dichlorobenzene for 150 hours. Refluxing for only 5 hours in *o*-dichlorobenzene containing alumina served to convert the *N*-methylindanthrone into indanthrone. The colouring matter became adsorbed on the alumina.

(*d*) A column of cellulose was prepared from a suspension of cellulose pulp (Whatman No. 1 filter paper) in a large volume of water. The column was washed with a solution containing sodium hydroxide (1%) and sodium dithionite (0·5%) in boiled-out distilled water. A solution prepared from the blue product and alkaline dithionite was then poured on the column. Two zones developed and were eluted by alkaline dithionite. The more mobile orange-brown band yielded a clear solution having the same colour, from which *N*-methylindanthrone separated on exposure to air. The identity of the

product was confirmed by means of its absorption spectrum in pyridine, and by the green colour which resulted when methanolic potassium hydroxide was added to the pyridine solution (Fig. 1). The less mobile zone was blue; it consisted of indanthrone.

The product of experiment 7 was similarly shown to consist of indanthrone and *N*-methylindanthrone by differential absorption of the reduced forms on cellulose.

A synthetic mixture of indanthrone (0·05 g.) and *N*-methylindanthrone (0·05 g.; prepared from 2-amino-1 : 2′-dianthraquinonyl-*N*-methylamine) was similarly shown to be separable on a column of cellulose.

Self-condensation of 1-*Chloro*-2-*methylaminoanthraquinone.*—(*a*) A solution containing 1-chloro-2-methylaminoanthraquinone (2·0 g.) in nitrobenzene (20 c.c.) was heated under reflux with copper sulphate (0·05 g.) and potassium acetate (1·25 g.) for 24 hours. The solution was filtered hot from a negligible residue. The brown filtrate was distilled in steam; a residue (1·9 g.; m. p. 170—180°) remained. A portion of this product was heated with acetic anhydride; it gave yellow crystals, m. p. 258°, which, recrystallised from acetic acid, formed needles, m. p. 265°, alone or mixed with 2-acetamidoanthraquinone. The remainder of the product was chromatographed in benzene on alumina. The main zone was orange-red; extracted with acetone it yielded reddish-brown needles of 2-methylaminoanthraquinone, m. p. 232—233°. Acetylation gave 2-*N*-methylacetamidoanthraquinone, m. p. 156°.

(*b*) When in (*a*) the condensing agent employed was sodium acetate (3 g.) and cupric chloride (0·25 g.) in nitrobenzene (50 c.c.), the cuprous derivative of *NN*′-di-2-anthraquinonylformamidine (0·9 g.) was obtained. The total ionised chloride yielded 3·02 g. of silver chloride, indicating that complete dehalogenation of the 1-chloro-2-methylaminoanthraquinone had occurred.

The same cuprous derivative was also obtained when the condensing agents were sodium acetate and cupric acetate and the medium *o*-dichlorobenzene.

The authors thank the University of Leeds for the award of a Clothworkers Research Scholarship and the Trustees of Messrs. Courtaulds' Scientific and Educational Trust Fund for the award of a grant to one of them (E. L.). They also thank Imperial Chemical Industries Limited for gifts of intermediates and grants to meet the cost of microanalyses.

Clothworkers Research Laboratory,
University of Leeds. [*Received, February 27th,* 1951.]

---

472. *Chemistry of Indanthrone. Part III.* The Cyclisation of 2-Amino-1 : 2′-dianthraquinonylamine.*

By William Bradley, Edward Leete, and Douglas S. Stephens.

Stannous chloride reduction of 2-nitro-1 : 2′-dianthraquinonylamine affords 2-amino-1 : 2′-diantfiraquinonylamine and indanthrone. The latter product is formed when the former is heated alone, in air or carbon dioxide, in acetic acid, or in pyridine containing potassium hydroxide. A suspension of sodium hydroxide in cold pyridine converts the 2-amino-compound into a grey-green intermediate which is changed into indanthrone by heating it in quinoline. The intermediate is considered to be a hydroaromatic compound formed by linking the 2-amino-group to the 1-position of the adjacent nucleus. It is converted into indanthrone as a result of a prototropic change and dehydrogenation. The 2-methylamino-analogue cyclises with equal ease to form *N*-methylindanthrone but the conversion of 2-amino-1 : 2′-dianthraquinonyl-*N*-methylamine into *N*-methylindanthrone requires the use of alkalis.

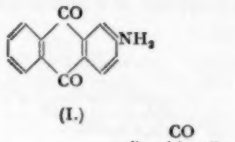
Reduction of the nitro-compound by alkaline dithionite yields 2-aminoanthraquinone and 2-aminoanthraquinol. The result indicates that in the process of forming indanthrone the initial step by which the 2-anthraquinonylamine anion becomes linked to the 1-position of another molecule of 2-aminoanthraquinone is reversible.

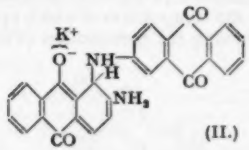
The reversible character of the first step in the sequence of changes which lead ultimately to indanthrone is considered to explain the increasing importance of the direct hydroxylation of 2-aminoanthraquinone, which leads to alizarin, with reduction in the temperature of the alkali fusion.

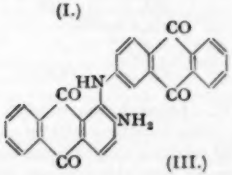
The present communication is concerned with the properties of 2-amino-1 : 2′-dianthraquinonylamine (III) and their bearing on the formation of indanthrone (IV) when 2-aminoanthraquinone (I) is heated with fused alkali hydroxides. In Part I (*J.*, 1951, 2129) it

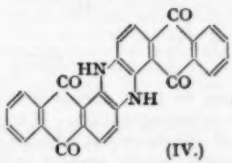
* Part II, preceding paper.

was shown that 2-aminoanthraquinone behaves as a weak acid towards strong alkalis, and also that the same compound and its *N*-aryl derivatives undergo substitution at the 1-position by the anions of certain weak acids, hydrogen being replaced. The facts support the view that (II), the adduct formed by the anion of the 2-anthraquinonylamine ion with 2-aminoanthraquinone represents an intermediate stage in the process of forming indanthrone from 2-aminoanthraquinone. Equally, the facts harmonize with the view first put forward by Barnett ("Anthracene and Anthraquinone," London, 1921, p. 344) that 2-amino-1 : 2′-dianthraquinonylamine (III) is an intermediate, since (III) can be derived from (II) by dehydrogenation by air, alkali nitrates, or the quinones, for example, 2-aminoanthraquinone, which are always present in the alkali melt.


(I.)

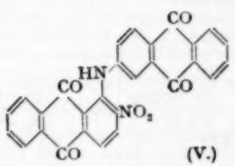

(II.)

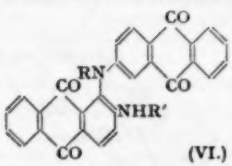

(III.)


(IV.)

In the preparation of (III), 2-acetamido-1-chloroanthraquinone was heated with 2-aminoanthraquinone, potassium acetate, and a copper catalyst in nitrobenzene. Dehalogenation occurred, 2-acetamidoanthraquinone being formed. Kopetschni and Wiesler (*Monatsh.*, 1922, **43**, 92) similarly found that 2-amino-1-chloroanthraquinone yielded 2-aminoanthraquinone when it was heated in dimethylaniline with cupric acetate.

1-Chloro-2-nitroanthraquinone, prepared by Kopetschni's method (G.P. 363,930) and also by the procedure described in Part I (*loc. cit.*), was condensed with 2-aminoanthraquinone as described in G.P. 581,439, to form 2-nitro-1 : 2′-dianthraquinonylamine (V). Reduction with stannous chloride in acetic acid afforded both the related amine (III) and indanthrone (IV). The conversion of the amine (III) into indanthrone was described in G.P. 544,919—by heating the amine in 1-nitronaphthalene or by passing a rapid current of air through its solution in α-chloronaphthalene. The present experiments have shown, however, that added oxidants are

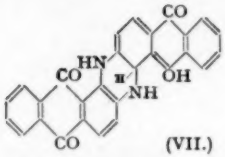

(V.)

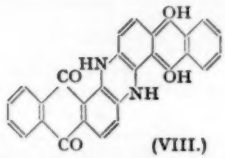

(VI.)

not essential for cyclisation, which takes place readily under a variety of conditions. It occurs when the amine is heated alone at 290°, or suspended in paraffin at this temperature. It does not occur in boiling pyridine, but it takes place readily when potassium hydroxide is added to a solution of the amine in cold pyridine. Indanthrone is also formed when the amine is heated with glacial acetic acid; in this respect 2-amino-1 : 2′-dianthraquinonylamine differs from both 2-amino-1 : 2′-dianthraquinonyl-*N*-methylamine (VI; R = Me, R′ = H) and its methyl derivative (VI; R = R′ = Me) which require the use of alkalis for their cyclisation to methylindanthrones. That the *tertiary* methyl group contributes to the different behaviour of the two methyl derivatives is shown by the properties of 2-methylamino-1 : 2′-dianthraquinonylamine (VI; R = H, R′ = Me) which cyclises to form *N*-methylindanthrone even in acid solution (preceding paper).

Lithium hydroxide, added to a solution of 2-amino-1 : 2′-dianthraquinonylamine in pyridine, had almost no action. Addition of powdered sodium hydroxide caused the rapid formation of a

grey-green substance (A). This product was not an alkali salt. It was insoluble in water, but sparingly soluble in *o*-dichlorobenzene with a greenish-yellow colour; it formed a reddish-brown solution in concentrated sulphuric acid, from which it was precipitated unchanged by water. It dissolved in pyridine with a dull green colour; on addition of methanolic potassium hydroxide a deep green colour resulted. A deep green colour with the same reagent is also given by the three isomeric dianthraquinonylamines and certain other –NH– compounds, including 2-anilinoanthraquinone (*J.*, 1951, 2133). Indanthrone was formed merely by heating (A) with boiling quinoline (cf. Fig.), an indication that (A) is not an anthrone or anthranol; compounds belonging to these types are oxidised to indanthrone only with difficulty. Warming (A) with alkaline dithionite (hydrosulphite) dissolved it, forming the blue alkali salt of dihydroindanthrone and subsequent aeration of the solution caused the separation of indanthrone. These properties suggest that (A), the composition of which approximated closely to that of a dihydroindanthrone, is a compound having the constitution (VII), which is capable of a prototropic change in the

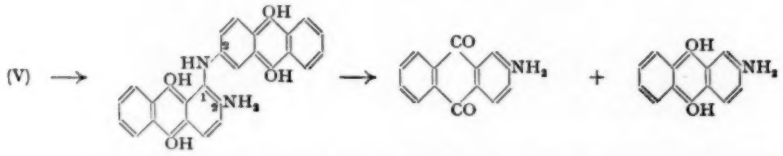

(VII.)


(VIII.)

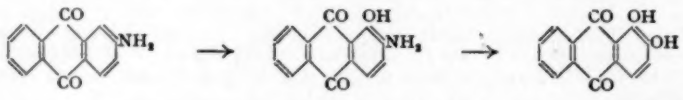
presence of bases to form dihydroindanthrone (VIII). Indanthrone is very readily derived from (VIII) by dehydrogenation. It is probable that other instances will be encountered in the present group of compounds in which a hydroaromatic nucleus results from the attachment of an electron-donating group, present in a side chain, to an aromatic nucleus, the process being analogous to the formation of *pseudo*-bases by the action of alkalis on heterocyclic 'onium salts.

Heating 2-amino-1 : 2′-dianthraquinonylamine at 290° in an atmosphere of carbon dioxide gave indanthrone but no alkali-soluble product. A similar result was obtained when 2-amino-1 : 2′-dianthraquinonylamine was heated with potassium hydroxide in pyridine containing methyl alcohol.

When the related nitro-compound (V) was reduced with alkaline dithionite, the initial product decomposed, yielding 2-aminoanthraquinone and 2-aminoanthraquinol. The reaction involves the elimination of the 2-anthraquinonylamino-substituent from the 1-position of the 2-aminoanthraquinol nucleus to which it is attached. The result is important for the present theory of formation of indanthrone which postulates the occurrence of a reduced form (II) of 2-amino-1 : 2′-dianthraquinonylamine as an intermediate. It indicates the weakness of the bond linking the secondary nitrogen to the 1-position of the aminated nucleus; it establishes further that the formation of the bond is a reversible process.



The reversible character of the initial substitution step, as a result of which the 2-anthraquinonylamine anion becomes linked to the 1-position of another molecule of 2-aminoanthraquinone, probably explains the observation, made first by Bohn (G.P. 129,845), that indanthrone is formed most abundantly when the temperature of the alkali fusion is 200—300°. At lower



temperatures alizarin is formed in notable amount; at 180° it forms 18% of the product (Liebermann, *Annalen*, 1882, **212**, 63). The direct hydroxylation of 2-aminoanthraquinone

leading first to 2-amino-1-hydroxyanthraquinone and then to alizarin is not a reversible process, and below 200° it represents an important side-reaction. At higher temperatures the rate of substitution by hydroxyl and by 2-anthraquinonylamine anions increases and indanthrone formation becomes favoured because of the stability of the end-product and the rate at which it is formed.

The simultaneous formation of alizarin and indanthrone by the alkali fusion of 2-aminoanthraquinone recalls the simultaneous formation of 4- and 6-hydroxy*meso*benzanthrones together with violanthrone when *meso*benzanthrone is submitted to alkali fusion. These processes are considered to involve two simultaneous reactions: (*a*) the direct hydroxylation of *meso*benzanthrone by hydroxyl ions, and (*b*) substitution into *meso*benzanthrone by the 4-*meso*benzanthronyl ion, hydrogen being replaced.

Experimental.

2-Acetamido-1-chloroanthraquinone. Dehalogenation.—A mixture of 2-acetamido-1-chloroanthraquinone (3 g.) (Junghans, *Annalen*, 1913, **399**, 320), potassium acetate (3 g.), copper bronze (0·1 g.), and cupric acetate (0·1 g.) in nitrobenzene (40 c.c.) was heated under reflux for 6 hours. The solvent was distilled in steam and the residue extracted by acetic acid. On cooling, the brown extract afforded 1·2 g. of an amorphous solid, m. p. 250—260°. Sublimed at 200° (bath)/0·5 mm. this afforded yellow needles (0·3 g.), m. p. 264—265°, not depressed on admixture with 2-acetamidoanthraquinone. When it was warmed with concentrated sulphuric acid and the resulting solution added to water the product yielded 2-aminoanthraquinone, m. p. 301—302°. There was no indication of the formation of a derivative of 1 : 2′-dianthraquinonylamine when 2-acetamido-1-chloroanthraquinone was heated with 2-aminoanthraquinone in naphthalene or quinoline.

2-Amino-1 : 2′-dianthraquinonylamine.—2-Nitro-1 : 2′-dianthraquinonylamine (2·0 g.; G.P. 581,439; *J.*, 1951, 2139) was finely powdered and then added to a boiling solution of AnalaR stannous chloride (4·0 g.) in glacial acetic acid (40 c.c.). After 5 minutes the solution was cooled, and the reddish-brown needles (1·9 g.) were collected and chromatographed in chlorobenzene on alumina. Development by the same solvent afforded three main zones. The most strongly adsorbed was violet-blue; eluted by means of quinoline this afforded indanthrone. The least strongly adsorbed was orange; elution with acetone yielded 0·2 g. of unchanged 2-nitro-1 : 2′-dianthraquinonylamine. The intermediate zone was violet; extraction by ethyl acetate yielded a red solution from which reddish-brown needles of *2-amino-1 : 2′-dianthraquinonylamine* (0·9 g.) (Found: C, 75·1, 7·50; H, 4·0, 3·8; N, 6·5, 6·4. $C_{28}H_{14}O_4N_2$ requires C, 75·7; H, 3·6; N, 6·3%) separated on evaporation. 2-Amino-1 : 2′-dianthraquinonylamine is red when powdered, dissolves in alkaline dithionite with a brown colour, and decomposes at 290°, without melting.

Reduction of 2-Nitro-1 : 2′-dianthraquinonylamine. Formation of 2-Aminoanthraquinone.—Sodium hydroxide (4 g.) and sodium dithionite (9 g.) in water (120 c.c.) at 65° were added to a paste of the finely divided nitro-compound (1·4 g.) and alcohol (10 c.c.). The mixture was heated to boiling for 30 minutes in a flask provided with a Bunsen valve. A red solution formed but this became yellow and a yellow precipitate separated. The solid was collected, washed with water, and recrystallised from acetic acid. Needles, m. p. 302°, not depressed by authentic 2-aminoanthraquinone, were obtained.

Cyclisation of 2-Amino-1 : 2′-dianthraquinonylamine. Formation of Indanthrone and an Intermediate Product.—(*a*) A red solution of the amine (0·05 g.) in glacial acetic acid (5 c.c.) became almost colourless after 3 hours' boiling; meanwhile violet needles of indanthrone separated.

(*b*) A similar change from red to blue occurred when the amine was heated to 320° in liquid paraffin.

(*c*) The amine (0·1 g.) was recovered unaltered after 10 hours' boiling with pyridine (5 c.c.).

(*d*) The amine (0·2 g.) was dissolved in pyridine (5 c.c.). Powdered lithium hydroxide was added and the suspension shaken occasionally during 10 days at the room temperature. Only a trace of indanthrone was formed; the bulk of the amine was recovered.

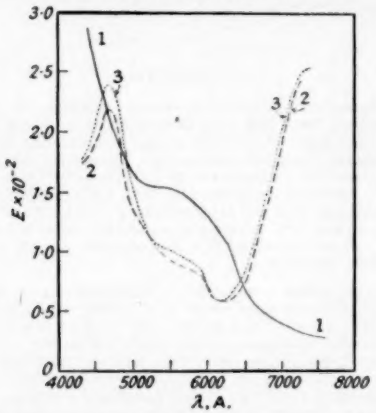
(*e*) In a similar experiment powdered potassium hydroxide (0·2 g.) was added to a solution of the amine (0·2 g.) in pyridine (5 c.c.); a green colour developed immediately. After 10 days at the room temperature methyl alcohol was added and the bluish-green product (0·195 g.) collected. This was dissolved in alkaline dithionite, and the solution passed through a column of cellulose, the method described in Part II (preceding paper) being used. The most strongly adsorbed zone was blue; it yielded indanthrone when eluted by alkaline dithionite and oxidised in air. There was also a weakly adsorbed brown zone. Similar treatment of this afforded *ca.* 0·005 g. of unchanged 2-amino-1 : 2′-dianthraquinonylamine, identified by its deep violet colour in concentrated sulphuric acid.

(*f*) In a similar experiment in which powdered sodium hydroxide (0·2 g.) was used instead of potassium hydroxide, the solution became green immediately and a green mass formed during 10 days at the room temperature. Methyl alcohol was added, the pale green product was collected, washed with water, and dried in air (yield, 0·16 g.) (Found: C, 73·4; H, 3·3; N, 6·3. $C_{28}H_{14}O_4N_2$ requires C, 75·7; H, 3·6; N, 6·3%). Heating this product (0·05 g.) with quinoline (30 c.c.) at the b. p. for 5 minutes changed the brown colour of the solution to greenish-blue; on cooling the characteristic curved needles of indanthrone (0·045 g.) separated. The pale green product dissolved in *o*-dichlorobenzene with a

greenish-yellow colour. It formed a reddish-brown solution in concentrated sulphuric acid (see figure); addition of water precipitated the pale green product unaltered. When kept it became bluer. It dissolved in alkaline dithionite with a deep blue colour; oxidation by air gave indanthrone in quantitative yield. The grey-green product dissolved in pyridine with a dull green colour; on addition of methanolic potassium hydroxide the solution became deep green.

(*g*) A few mg. of 2-amino-1 : 2′-dianthraquinonylamine were heated in an atmosphere of carbon dioxide at 300° for 15 minutes. The blue product was cooled in a stream of the gas and then added to 0·5 c.c. of 10% sodium hydroxide solution which had been boiled to expel air. There was no indication of the presence of an alkali-soluble product or of unchanged amine; the product contained indanthrone.

Products in concentrated sulphuric acid.



1, *Product obtained by the ring closure of* 2-amino-1 : 2′-*dianthraquinonylamine with sodium hydroxide in pyridine.*
2, *Product obtained by refluxing that of* (1) *with quinoline.*
3, *Indanthrone, max. at* 4650 Å. ($E = 240$), *min. at* 6150 Å. ($E = 61$).

(*h*) In the experiments recorded in the Table 2-amino-1 : 2′-dianthraquinonylamine was added to pyridine containing 3% (by vol.) of water. Powdered potassium hydroxide was added, and the containing vessels were evacuated until the medium boiled, and then closed. The reactants were shaken at the temperatures stated for the times recorded and then opened under warm, boiled-out water. In no instance was there evidence of the presence of a reduced (anthraquinol) form of indanthrone, which is known to dissolve in warm dilute sodium hydroxide with a deep blue colour. The resulting suspension was filtered off, washed with water, and dried. It was then extracted by hot pyridine (100 c.c.), and the undissolved material washed with hot pyridine and alcohol. The residue consisted of indanthrone; the extracts consisted mainly of unchanged amine and small amounts of indanthrone.

Temp.	16°	25°	35°	45°	70°	80°
2-Amino-1 : 2′-dianthraquinonylamine (g.)	0·4	0·4	0·4	0·4	0·4	0·4
Aqueous pyridine (c.c.)	20	20	20	20	30	40
KOH (g.)	2·0	2·0	2·0	2·0	4·0	6·0
Indanthrone (g.)	0·3	0·3	0·35	0·38	0·4	0·4
Products sol. in C_5H_5N (g.)	0·1	0·1	0·05	0·02	—	—
Reaction time (hrs.)	8	6	4	3	1	0·5

The authors thank the University of Leeds for the award of a Clothworkers Research Scholarship, and the Trustees of Messrs. Courtaulds' Scientific and Educational Trust Fund for the award of a grant to one of them (E. L.).

THE CLOTHWORKERS RESEARCH LABORATORY,
UNIVERSITY OF LEEDS.

[*Received, February 27th,* 1951.]

473. *Chemistry of Indanthrone. Part IV.* An Isomer of Indanthrone and the Constitution of Indanthren B.*

By WILLIAM BRADLEY, EDWARD LEETE, and DOUGLAS S. STEPHENS.

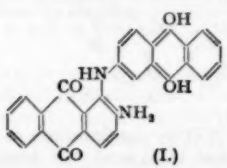
Whilst the reduction of 2-nitro-1 : 2′-dianthraquinonylamine with stannous chloride in acetic acid yields the related amine (A), reduction by means of sodium sulphide yields *NN*-dihydro-1 : 2-2′ : 3′-anthraquinoneazine (B), an isomer of indanthrone. The structure of the product is proved by its formation by condensing anthra-1 : 2-quinone with 2 : 3-diaminoanthraquinone, oxidising the resulting azine (C) to 1 : 2-2′ : 3′-anthraquinoneazine (D) and finally reducing this to the dihydro-azine. The azine (D) resembles indanthroneazine closely but 1 : 2-anthracene-2′ : 3′-anthraquinoneazine (C) is much more stable towards reduction.

The formation of (B) cannot involve the intermediate formation of (A) because (A) is known to form indanthrone on cyclisation (preceding paper). It is probable that 2-nitro-1 : 2′-dianthraquinonylamine becomes reduced to the related nitroso-compound which then cyclises to form the indanthrone isomer (B) before further reduction takes place.

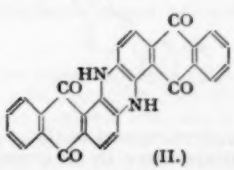
Indanthren B resembles (B) but the two colouring matters are not identical. The possibility that indanthren B is formed from (B) by the action of alkalis has been considered and shown to be improbable. It is suggested that indanthren B is a hydroxy- or dihydroxy-derivative of *NN*-dihydro-2 : 3-2′ : 3′-anthraquinoneazine.

A method of purifying indanthren B is described in which the reduced form is chromatographed on cellulose and the colouring matter regenerated by aeration.

AFTER his original description of the preparation of indanthrone (G.P. 129,845) by alkali fusion of 2-aminoanthraquinone, Bohn referred in G.P. 135,407 to the simultaneous formation of a distinct colouring matter which resembled indanthrone and which he named "indanthren B." The formation of "indanthren B" was favoured by addition of alcohol and similar reducing agents to the alkali melt (G.P. 135,408). The new colouring matter was stated to be more soluble than indanthrone in quinoline, to give a brownish-red solution when reduced by means of alkaline dithionite (hydrosulphite), and to be regenerated from its reduced form on aeration with greater difficulty than was indanthrone. Like indanthrone it yielded a yellow azine on oxidation, from which the original colouring matter was re-formed on reduction. Maki (*J. Soc. Chem. Ind. Japan, Suppl.*, 1933, **36**, 44) showed that "indanthren B" resulted even when pure 2-aminoanthraquinone was used and that its formation could not be attributed to the



(I.)



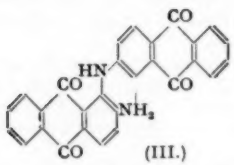
(II.)

presence of an initial impurity. Tanaka (*J. Chem. Soc. Japan*, 1935, **56**, 192) obtained a green product by heating 2-aminoanthraquinone with fused alkalis. He referred to it as "indanthren B" and stated that it was a quinol-quinone (I) and that it was converted into indanthrone (II) when heated again with fused alkali. "Indanthren B" cannot have the constitution (I), however, because of its colour, and because (I) dissolves readily in aqueous sodium hydroxide forming a brown solution (*J.*, 1951, 2161). In G.P. 347,692 a method of purifying crude indanthrone is described and it is stated that one of the impurities is a reduction product of indanthrone. Schwenk (*Chem.-Ztg.*, 1928, **52**, 45) held that "indanthren B" was a reduced form of indanthrone. This view does not accord with the known properties of "indanthren B,"

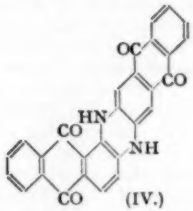
* Part III, preceding paper.

confirmed in the present experiments, that " indanthren B " and indanthrone cannot be interconverted by processes of oxidation and reduction. " Indanthren B " prepared by Maki's procedure (*loc. cit.*) was purified by dissolution in alkaline dithionite and passage of the solution through a column of cellulose prepared as in Part II (*J.*, 1951, 2147). " Indanthren B " was less strongly adsorbed than the indanthrone which was also present, and was easily eluted by means of alkaline dithionite as a brown solution from which aeration precipitated the purified " indanthren B " in the form of blue flocks. The properties of the product were similar to those of the original " indanthren B " described in G.P. 135,407. Oxidation with nitric acid or chromium trioxide gave a yellow product from which the original colouring matter was regenerated on reduction (see Fig. 1). The effect of alcohol in favouring the formation of " indanthren B " has been confirmed in the present work. In colour and absorption spectrum in concentrated sulphuric acid " indanthren B " resembled indanthrone closely, but analysis showed it to be richer in oxygen.

The present view that the formation of indanthrone from 2-aminoanthraquinone involves 2-amino-1 : 2′-dianthraquinonylamine (III) or a reduced form of this at an intermediate stage



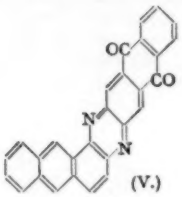
(III.)



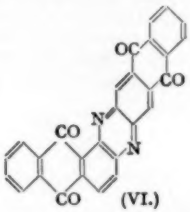
(IV.)

(preceding paper) suggested the possibility that cyclisation might not have proceeded solely to give indanthrone but that an isomer (IV) might have resulted by ring-closure at the 3-position. There was the possibility that " indanthren B " was (IV) or a derivative of this.

Terres (*Ber.*, 1913, **46**, 1634) and G.P. 170,562 described a synthesis of indanthrone in which 1 : 2-diaminoanthraquinone was condensed with anthra-1 : 2-quinone, and the resulting 1 : 2-anthracene-1′ : 2′-anthraquinoneazine was oxidised to indanthroneazine and then reduced to indanthrone. We applied the same procedure to prepare the indanthrone isomer (IV). 2 : 3-Diaminoanthraquinone was condensed with anthra-1 : 2-quinone and the resulting 1 : 2-anthracene-2′ : 3′-anthraquinoneazine (V) was oxidised to 1 : 2-2′ : 3′-anthraquinoneazine



(V.)



(VI.)

(VI) and the product reduced to (IV). Preparation of (IV) by condensation of alizarin with 2 : 3-diaminoanthraquinone in the presence of phenol and boric acid was described in G.P. 178,130, but we were unable to prepare (IV) satisfactorily by this method. The azine (VI) resembles indanthroneazine closely in that it is reduced to the related dihydro-azine merely by being heated with quinoline. The two dihydroazines, however, behave differently on reduction. Indanthrone dissolves in warm alkaline dithionite, forming a blue solution from which indanthrone is rapidly reprecipitated on exposure to air; (IV) dissolves to a deep reddish-brown solution from which the original colouring matter is precipitated more slowly than is indanthrone on aeration, and through a dull violet, and a greenish-yellow stage in succession. The final stage of change to blue colouring matter is slow in the case of (IV) because (IV) is a relatively strong acid which affords an alkali salt. When the greenish-yellow stage has been reached, addition of dilute acid precipitates the blue colouring matter. The alkali-salt forming properties of (IV) accord with the results described in Part I, in particular with the fact that

1-anilinoanthraquinone does not show any change in colour when methanolic potassium hydroxide is added to a solution in pyridine whilst 2-anilinoanthraquinone shows a colour change from orange to green (*J.*, 1951, 2129) and there can be little doubt that the potassium salt is the derivative (VII). *NN*-Dihydro-1 : 2-2′ : 3′-anthraquinoneazine affords a dimethyl derivative on methylation. This resembles *NN*-dimethylindanthrone in dissolving in pyridine with a blue colour which is unaltered by methanolic potassium hydroxide. It dissolves in alkaline dithionite, forming an orange-red solution from which the original colouring matter is regenerated in a single stage; in this respect the dimethyl derivative differs from the parent *NN*-dihydro-1 : 2-2′ : 3′-anthraquinoneazine. The dimethyl derivative resembles *NN*-dimethylindanthrone further in undergoing demethylation when heated with alumina, and in being more soluble in organic solvents than the unmethylated dihydro-azine. The isomer of

FIG. 1. FIG. 2. FIG. 3.

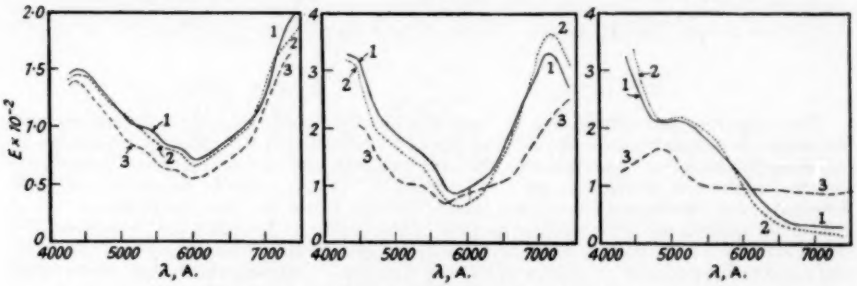


FIG. 1.—*Indanthren B in concentrated sulphuric acid.*

1, *Indanthren B obtained by fusion of 2-aminoanthraquinone in the presence of phenol, max. at* 4400 Å. ($E = 147$), *min. at* 6000 Å. ($E = 74$).
2, *Product obtain by oxidation of the above, followed by reduction.*
3, *Indanthren B obtained by fusion of 2-aminoanthraquinone in the presence of alcohol, max. at* 4400 Å. ($E = 138$), *min. at* 6000 Å. ($E = 54$).

FIG. 2.—*Solution of* NN-*dihydro*-2 : 1-2′ : 3′-*anthraquinonazine in concentrated sulphuric acid.*

1, NN′-*Dihydro*-1 : 2-2′ : 3′-*anthraquinoneazine prepared from* 2 : 3-*aminoanthraquinone, min. at* 5850 Å. ($E = 87$), *max. at* 7150 Å. ($E = 330$).
2, *Product obtained by reduction of* 2-*nitro*-1 : 2′-*dianthraquinonylamine with alcoholic sodium sulphide.*
3, *Product obtained by reduction of* 2-*nitro*-1 : 2′-*dianthraquinonyl*-N-*methylamine, min. at* 5700 Å. ($E = 72$).

FIG. 3.—*Solutions in sodium hydroxide–sodium dithionite of :*

1, NN′-*Dihydro*-1 : 2-2′ : 3′-*anthraquinoneazine prepared from* 2 : 3-*diaminoanthraquinone, min. at* 4900 Å. ($E = 206$), *max. at* 5200 Å. ($E = 212$).
2, *Product obtained by reduction of* 2-*nitro*-1 : 2′-*dianthraquinolylamine with alcoholic sodium sulphide.*
3, *Indanthren B, max. at* 4850 Å. ($E = 160$).

indanthrone (IV) is probably the main constituent of the colouring matter obtained by heating 3-nitro-2 : 1′-dianthraquinonylamine with methanolic potassium hydroxide (G.P. 583,715).

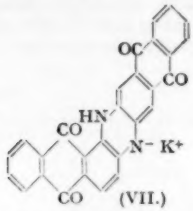
" Indanthren B " resembles (IV) in colour, colour in sulphuric acid, and in dissolution in alkaline dithionite. It differs from (IV) in dissolving in pyridine with a blue colour which is changed to green by methanolic potassium hydroxide; with (IV) the corresponding colour change is from blue to greenish-brown.

The possibility that " indanthren B " is derived from (IV) by the further action of fused alkali hydroxides has been investigated. It was found that (IV) was recovered unaltered. When potassium acetate and potassium nitrate were added to the melt gross decomposition occurred resulting in the formation of a reddish-brown product.

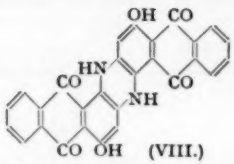
A view that " indanthren B " is a mono- or di-hydroxy-derivative of (IV) accords with its composition and general properties but the failure to obtain it by further action of fused alkalis on *NN*-dihydro-1 : 2-2′ : 3′-anthraquinoneazine, alone or in the presence of oxidants, suggests that the view is incorrect.

A careful comparison of the stabilities towards hydrolysis of the colours produced when methanolic potassium hydroxide is added to pyridine solutions of numerous anthraquinone

derivatives and related compounds has made it clear that " indanthren B " is a phenolic compound. The most acidic –NH– compounds encountered in the survey were the various anthraquinoneacridones but these did not approach " indanthren B " in the stability of their alkali salts. On the other hand " indanthren B " did resemble the hydroxyanthraquinones and 4 : 4′-dihydroxyindanthrone (VIII). The behaviour of the last-mentioned is especially interesting. It is very sparingly soluble in pyridine but on addition of methanolic potassium hydroxide a green solution is formed which in colour and stability towards hydrolysis closely resembles " indanthren B."

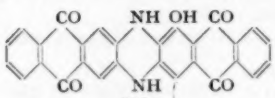


(VII.)

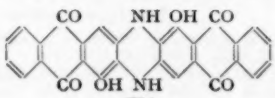


(VIII.)

The properties and composition of " indanthren B " accord best with its formulation as the mono- or di-hydroxy-derivative (IX or X), of *NN*-dihydro-2 : 3-2′ : 3′-anthraquinoneazine, the linear isomeride of indanthrone. This view accords with the properties of indanthrone and its isomers and derivatives, for " indanthren B," though phenolic, is redder than *NN*-dihydro-1 : 2-2′ : 3′-anthraquinoneazine, which in turn is redder than indanthrone. 4 : 4′-Dihydroxyindanthrone is the greenest member of the series. " Indanthren B " resembles *NN*-dihydro-1 : 2-2′ : 3′-anthraquinoneazine rather than indanthrone in its strongly acid character, and in the brown colour of its solution in alkaline dithionite. All indanthrone derivatives which

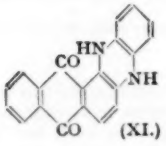


(IX.)

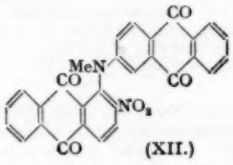


(X.)

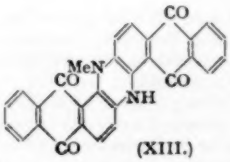
are able to dissolve in this medium whilst still containing the grouping (XI) afford blue solutions, whereas *N*-methyl- and *NN*-dimethyl-indanthrone as well as fully reduced indanthrone which do not contain this grouping afford brown solutions. This relationship between structure and the colour of the alkaline solution of the reduced form, together with the close similarity of *NN*-dihydro-1 : 2-2′ : 3′-anthraquinoneazine and " indanthren B," supports the view that the latter is derived from the linear isomeride of indanthrone.



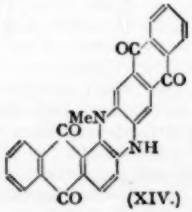
(XI.)



(XII.)



(XIII.)



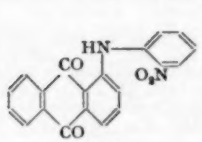
(XIV.)

Whilst the reduction of 2-nitro-1 : 2′-dianthraquinonylamine with stannous chloride affords (III) (Part III, preceding paper), reduction with alcoholic sodium sulphide follows a different

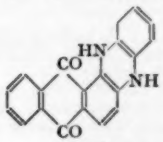
course and yields the isomer (IV) of indanthrone. The identity of the product with (IV) was confirmed by analysis, absorption spectrum in concentrated sulphuric acid, colour of its solution in alkaline dithionite (see Figs. 2 and 3), and by the greenish-brown colour developed when methanolic potassium hydroxide was added to a solution of the product in pyridine. When the reduction was carried out by aqueous sodium sulphide the yield of (IV) was smaller. The product contained unreduced nitro-compound but neither indanthrone nor 2-aminoanthraquinone.

The reduction of 2-nitro-1 : 2′-dianthraquinonyl-*N*-methylamine (XII) by aqueous sodium sulphide yielded a blue colouring matter which was not identical with *N*-methylindanthrone (XIII). By analogy with the product obtained from 2-nitro-1 : 2′-dianthraquinonylamine and sodium sulphide that derived from (XII) should be (XIV), a *N*-methyl derivative of the indanthrone isomer (IV). This conclusion is supported by the absorption spectrum of (XIV) in sulphuric acid which closely resembles that of (IV) (see Fig. 3).

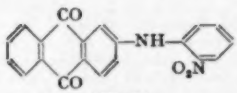
In this connection reference must be made to the proof by Ullmann and Fodor (*Annalen*, 1911, **380**, 324) that 1-*o*-nitroanilinoanthraquinone (XV) is reduced by alcoholic sodium sulphide to *NN*-dihydro-3 : 4-phthaloylphenazine (XVI). In the present work it was found



(XV.)



(XVI.)



(XVII.)

that 2-*o*-nitroanilinoanthraquinone (XVII), similarly reduced, did not yield the dihydrophenazine (XVI), but a product, probably the related amine, which proved to be stable towards ring closure with alkali and sodium sulphide. Evidently the cyclisation of (XV) to (XVI) occurs before the related amine is formed, and a similar conclusion must be reached regarding the sodium sulphide reduction of 2-nitro-1 : 2′-dianthraquinonylamine. In this instance it is known that the related amine (III) yields indanthrone on ring closure, whereas the product obtained by reducing the nitro-compound with sodium sulphide is the indanthrone isomer (IV), neither the related amine nor indanthrone being formed.

2-Nitro-1 : 2′-dianthraquinonylamine forms a stable salt with potassium hydroxide (Part I, *J.*, 1951, 2139) but is not otherwise easily changed by this reagent. The effect of sodium sulphide added to the alkali is probably to reduce the nitro- to the related nitroso-compound which then undergoes cyclisation with formation of (IV). Probably the related nitroso-compounds are the intermediates which cyclise when 2-nitro-1 : 2′-dianthraquinonyl-*N*-methylamine (XII) and 2-*o*-nitroanilinoanthraquinone are reduced by sodium sulphide.

Experimental.

" Indanthren B."—(*a*) The product obtained by heating 2-aminoanthraquinone (10 g.) with potassium hydroxide (34 g.), water (6 c.c.) and phenol (6·0 g.) at 220° according to Maki's procedure (*loc. cit.*) weighed 0·35 g. It was dissolved in water (20 c.c.) containing sodium dithionite (1·0 g.) and sodium hydroxide (5 c.c. of 20%), and the brown solution was mixed with water containing sodium dithionite (1%) and sodium hydroxide (2%) and then passed through a column of cellulose pulp. A strongly adsorbed blue zone was succeeded by a lower, dull brownish-grey zone. The column was extruded and cut into thin sections and the adsorbed material was allowed to oxidise in air. The blue, strongly adsorbed zone yielded indanthrone. The brownish-grey zone became green and finally blue as oxidation proceeded; the blue product, extracted by *o*-dichlorobenzene, afforded 0·1 g. of blue needles (Found : C, 71·8; H, 3·4; N, 4·2. $C_{28}H_{14}O_5N_2$ requires C, 72·9; H, 3·5; N, 6·1. $C_{28}H_{14}O_6N_2$ requires C, 70·5; H, 3·4; N, 5·9%).

(*b*) 2-Aminoanthraquinone (10 g.) was added during 20 minutes to a molten mixture of potassium hydroxide (50 g.) and ethyl alcohol (25 c.c.) at 150°. The mass was stirred for 3 hours at this temperature and then added to water. The resulting deep violet solution was aerated and the precipitate (8·0 g.) collected. Extraction of the precipitate by alcohol gave a blue insoluble portion (2·7 g.). This was extracted by boiling nitrobenzene (200 c.c.); a portion (1·0 g.), which showed the reactions of indanthrone, remained undissolved. The filtrate afforded indistinct blue crystals (0·55 g.) on cooling; these differed from indanthrone in dissolving in alkaline dithionite with a brown colour. The brown solution in alkaline dithionite was passed through a column of cellulose pulp. As in (*a*), two zones formed, the upper blue zone yielded indanthrone, the lower greyish-brown zone afforded " indanthren B " which, extracted from the cellulose by pyridine and precipitated therefrom by alcohol, was obtained as an amorphous blue powder (0·19 g.). The blue pyridine solution of this product became bright green when methanolic potassium hydroxide was added, and the colour was stable towards dilution with

alcohol or even water; on storage a green precipitate was formed. Addition of a drop of hydrochloric acid restored the original blue colour.

In a modification of the test, "indanthren B" was heated with boiling pyridine, and two volumes of water were added and finally potassium hydroxide; a green colour developed and on storage a green precipitate. Even when heated with aqueous sodium hydroxide "indanthren B" dissolved to a slight extent forming a brownish-green solution.

Oxidation. (*a*) A solution of chromium trioxide (0·05 g.) in 80% sulphuric acid (2 c.c.) was added at 0° to one of "indanthren B" (0·05 g.) in concentrated sulphuric acid (1 c.c.). The mixture was stirred for an hour during which the colour of the solution changed from dull brown to reddish-brown. On addition of the mixture to water a blue-green precipitate formed; this was collected (centrifuge) and washed with very dilute sodium hydroxide containing sodium dithionite. Finally, it was washed thoroughly with water and dried. The product was identical with the starting material.

(*b*) "Indanthren B" (0·04 g.) was added at 0° to concentrated nitric acid (*d* 1·4; 1 c.c.). The orange-yellow solution was stirred for 15 minutes and then added to water. A yellow precipitate resulted; in contact with dilute sodium hydroxide it became blue; on addition of alkali and sodium dithionite and warming to 50° it dissolved with a brown colour. Oxidation by aeration and neutralisation by acid caused a greenish-blue precipitate (0·015 g.) to be formed. This was shown to be identical with the starting material by means of the absorption spectrum of the brown solution in concentrated sulphuric acid (see Fig. 1).

1 : 2-*Anthracene*-2′ : 3′-*anthraquinoneazine*.—1 : 2-Anthraquinone was obtained in small yield by reducing alizarin to 1 : 2-dihydroxyanthracene (Graebe, *Annalen*, 1906, **349**, 207; Hall and Perkin, *J.*, 1923, 2029) and oxidising the product by chromic acid. A better method consisted in preparing anthracene-2-sulphonic acid (cf. Ferrero and Conzetti, *Helv. Chim. Acta*, 1928, **11**, 1152), converting this in turn into 2-anthrol, 2-hydroxy-1-nitrosoanthracene, and 1-amino-2-hydroxyanthracene, and finally oxidation to 1 : 2-anthraquinone (Lagodzinski, *Annalen*, 1905, **342**, 87). After isolation of 2-anthrol the successive yields were almost quantitative.

A solution of 1 : 2-anthraquinone (2·0 g.) in glacial acetic acid (50 c.c.) was added to one of 2 : 3-diaminoanthraquinone (2·1 g.) in glacial acetic acid (500 c.c.). A product began to separate almost at once. After 30 minutes the suspension was cooled and the golden-yellow leaflets (2·9 g.) were collected. Recrystallisation from nitrobenzene gave 1 : 2-*anthracene*-2′ : 3′-*anthraquinoneazine* as golden-yellow plates, m. p. 415—417° (Found: C, 82·2; H, 3·6; N, 6·5. $C_{28}H_{14}O_2N_2$ requires C, 81·9; H, 3·4; N, 6·8%). It dissolved in concentrated sulphuric acid with a deep green colour; on storage a reddish-blue solid (sulphate?) separated; this decomposed when added to water, and a violet solution resulted and then a brownish-yellow precipitate. The azine was recovered unaltered when 1 g. was heated under reflux for 14 hours with 10 c.c. of quinoline. This stability is in sharp contrast with that of 1 : 2 : 1′ : 2′-anthraquinoneazine (indanthroneazine) which becomes reduced to indanthrone even when it is heated with nitrobenzene (Scholl and Berblinger, *Ber.*, 1903, **36**, 3427). In another experiment the azine (0·5 g.) was warmed with a solution of sodium hydroxide (2·0 g.) and sodium dithionite (2·0 g.) in water (50 c.c.). A portion dissolved with a reddish-brown colour, but after a short time a brown substance was precipitated. The filtered solution exposed to air gave a red precipitate. This was collected (centrifuge; 0·04 g.) and heated with nitrobenzene. It dissolved with a yellow colour and the solution afforded yellow plates of the original azine, m. p. 417°, on cooling. The brown precipitate, collected (0·35 g.) and then crystallised from nitrobenzene, afforded a yellow solution having a green fluorescence and on cooling golden-yellow plates of the azine, m. p. 416—417°.

NN-*Dihydro*-1 : 2-2′ : 3′-*anthraquinoneazine*.—(*a*) A solution prepared from chromium trioxide (1·0 g.) and water (2 c.c.) was mixed with concentrated sulphuric acid (10 c.c.) and then added at 0° to one of 1 : 2-anthracene-2′ : 3′-anthraquinoneazine (1·0 g.) in concentrated sulphuric acid (25 c.c.). There was an immediate change in colour from green to reddish-brown. The mixture was stirred for 15 minutes, then added to water, and the resulting greenish-yellow suspension warmed to 50° and then filtered. The green residue (1·35 g.) extracted for 3 hours by boiling quinoline (300 c.c.) yielded a greenish-blue solution from which on cooling very small blue needles (0·15 g.) separated (Found: C, 75·7; H, 3·5; N, 5·9. $C_{28}H_{14}O_4N_2$ requires C, 76·0; H, 3·2; N, 6·3%). The *dihydro-azine* afforded a bright blue solution in pyridine; on addition of methanolic potassium hydroxide the colour changed to dull greenish-brown. The brown colour is stable towards dilution with methanol or even water; a brown precipitate slowly forms. Addition of a drop of hydrochloric acid to the diluted solution restores the original blue colour.

The dihydro-azine can also be prepared from the sulphuric acid solution of the oxidised anthracene-anthraquinoneazine by addition to water, basification with sodium hydroxide, and then warming to 50° with the addition of 20% sodium hydroxide (8 c.c.) and sodium dithionite (2·0 g.). A brown solution formed; this was filtered off and the filtrate aerated. The resulting suspension was made neutral, and the fine precipitate collected, and washed with water and finally with dilute hydrochloric acid. The crude dihydro-azine (0·7 g.) so obtained dissolved in concentrated sulphuric acid with a greenish-brown colour; on addition of water it was reprecipitated as a dull blue solid. Nitric acid added to a solution of the dihydro-azine in concentrated sulphuric acid gave an orange-brown colour.

(*b*) Finely powdered 2-nitro-1 : 2′-dianthraquinonylamine (2·0 g.) was heated under reflux for 30 minutes with a solution of sodium sulphide crystals (5·0 g.) in alcohol (100 c.c.). A transient reddish-brown colour formed but this soon became bluish-green. The cooled product was filtered off and washed with alcohol and water. The blue residue was dissolved in alkaline sodium dithionite, and the resulting brown solution chromatographed on cellulose. A uniform brown zone was obtained which was less strongly adsorbed than reduced indanthrone but more strongly than reduced "indanthren B."

Recovered from the cellulose and recrystallised from 250 parts of boiling quinoline the NN-*dihydro*-1 : 2-2′ : 3′-*anthraquinoneazine* was obtained as blue needles (Found: C, 76·1; H, 3·4; N, 6·35. $C_{28}H_{14}O_4N_2$ requires C, 76·0; H, 3·2; N, 6·3%). When the dihydro-azine is reduced by alkaline dithionite and the brown solution is adsorbed on cellulose in contact with air the colour changes rapidly to dull bluish-violet and then almost at once to dull green. The final transition to blue occurs slowly unless acid is added, whereupon it takes place immediately. The same behaviour is shown by the dihydro-azine prepared by method (*a*).

The same dihydro-azine was obtained less conveniently by reducing 2-nitro-1 : 2′-dianthraquinonylamine with a solution of sodium sulphide in aqueous sodium hydroxide.

Alkali fusion. (*a*) The finely powdered dihydro-azine (1·0 g.) was stirred for an hour at 200° with a melt of potassium hydroxide (10·0 g.) and water (1·0 c.c.). The dark product added to water afforded a brown solution; there was no residue. The filtered solution when acidified yielded a dull blue precipitate (0·9 g.) consisting of the unchanged dihydro-azine. A portion of it was dissolved in alkaline dithionite and chromatographed on cellulose; only a single bright brown zone resulted.

(*b*) In a similar experiment potassium acetate (0·5 g.) and potassium nitrate (0·2 g.) were added to the melt before introduction of the dihydro-azine. On addition to water a brown solution was obtained and from this a reddish-brown product (0·7 g.).

9 : 10-*Dihydro*-9 : 10-*dimethyl*-1 : 2-6 : 7-*diphthaloylphenazine.*—The dihydro-azine (1·0 g; prepared by reducing 2-nitro-1 : 2′-dianthraquinonylamine with alcoholic sodium sulphide) was heated under reflux with methyl toluene-*p*-sulphonate (4·0 g.) and potassium carbonate (2·0 g.) in trichlorobenzene (100 c.c.) for 48 hours. The blue solution was filtered hot and the filtrate evaporated to 40 c.c. On cooling, crystals (0·7 g.) separated. Two recrystallisations from quinoline afforded the *phenazine* derivative as blue needles (0·3 g.) (Found: C, 74·1; H, 3·8; N, 6·0. $C_{30}H_{18}O_4N_2$ requires C, 76·6; H, 3·8; N, 6·0%). It dissolved readily in pyridine with a violet-blue colour which was unaltered by methanolic potassium hydroxide, whether in the cold or on heating. It dissolved in alkaline dithionite with an orange-red colour. Exposure to air regenerated the original violet-blue colour. Unlike the behaviour of the parent dihydro-azine there was no indication of a stable intermediate stage in the process of reoxidising the reduced methyl derivative.

When the *NN*-dimethyl derivative (0·05 g.) was heated under reflux for 10 hours in *o*-dichlorobenzene containing alumina (0·5 g.) and the suspension was allowed to cool, all the colouring matter was adsorbed on the alumina. Extracted from the alumina by means of pyridine, the adsorbed product afforded a deep blue solution which became olive-brown on addition of methyl-alcoholic potassium hydroxide. When the product was dissolved in alkaline dithionite the resulting brown solution yielded first a pale green solution and finally a blue colour on exposure to air. Both these reactions are characteristic of the demethylated amine.

Alkali Fusion of Indanthrone.—Indanthrone was recovered almost completely unaltered when 2·0 g. was heated for 30 minutes with potassium hydroxide (40 g.) and ethyl alcohol (20 c.c.) at 140—150°. The product, reduced and then chromatographed on cellulose, afforded a main blue zone consisting of dihydroindanthrone and a faint brown zone containing only a negligible amount of material (cf. Maki, *J. Soc. Chem. Ind. Japan, Suppl.*, 1929, **32**, 300).

2-*o*-*Nitroanilinoanthraquinone.*—2-Iodoanthraquinone (3·0 g.) was heated under reflux for 3 hours in nitrobenzene (20 c.c.) with *o*-nitroaniline (2·0 g.), lead monoxide (2·0 g.), and cupric acetate (0·05 g.). The hot suspension was filtered; on cooling the filtrate gave 2·25 g. of the product, m. p. 243—244°. Recrystallisation from acetic acid afforded orange-yellow needles, m. p. 247—248° (Found: C, 69·6; H, 3·6; N, 8·3. $C_{20}H_{12}O_4N_2$ requires C, 69·7; H, 3·5; N, 8·2%). 2-*o*-*Nitroanilinoanthraquinone* dissolved in pyridine with a yellow colour; addition of methanolic potassium hydroxide changed the colour to green and this was stable to considerable dilution with alcohol.

Reduction. 2-*o*-Nitroanilinoanthraquinone (1·0 g.) was heated under reflux for 30 minutes in alcohol (50 c.c.) containing sodium sulphide crystals (3·0 g.). The product added to water (300 c.c.) afforded a red crystalline precipitate, m. p. 220—230°. This was readily soluble in water and quite different in this respect from *NN*-dihydro-1 : 2-phthaloylphenazine (Ullmann and Fodor, *Annalen*, 1911, **380**, 324) obtained by the similar reduction of 1-*o*-nitroanilinoanthraquinone. Like the *o*-aminodianthraquinonylamines it dissolved in concentrated sulphuric acid with a deep violet-blue colour. In similar circumstances anthraquinonedihydroazines afford brown solutions.

The authors thank the University of Leeds for the award of a Clothworkers Research Scholarship and the Trustees of Messrs. Courtaulds' Scientific and Educational Trust Fund for the award of a grant to one of them (E. L.). They also thank Imperial Chemical Industries Limited for gifts of intermediates and grants to meet the cost of microanalyses.

CLOTHWORKERS RESEARCH LABORATORY,
UNIVERSITY OF LEEDS.

[*Received, February 27th*, 1951.]

474. *Chemistry of Indanthrone. Part V.** tert.-*Butyl Derivatives of Indanthrone and Flavanthrone. The Mode of Formation of Flavanthrone in the Alkali Fusion of 2-Aminoanthraquinone.*

By William Bradley and Harry E. Nursten.

The course of chemical change is frequently modified by the presence of bulky alkyl groups in one or more of the reactants. Fused with potassium hydroxide at 240°, 2-aminoanthraquinone yields indanthrone; at 300° the main product is flavanthrone. 2-Amino-3-*tert.*-butylanthraquinone yielded 3 : 3′-di-*tert.*-butylflavanthrone at both of these temperatures; there was no indication of the formation of 3 : 3′-di-*tert.*-butylindanthrone or the related azine. The indanthrone was prepared by the self-condensation of 2-amino-1-bromo-3-*tert.*-butylanthraquinone. The reaction yielded also the corresponding azine and flavanthrone. The formation of a flavanthrone derivative in a reaction of the kind described is very unusual.

Di-*tert.*-butylindanthrone is less stable than indanthrone towards dehydrogenation to an azine. The result accords with the known effect of alkyl groups in facilitating the dehydrogenation of 1 : 4-dihydroxynaphthalene to α-naphthaquinone. There is no evidence for a steric effect of *tert.*-butyl groups which restrains the dehydrogenation of indanthrone to indanthroneazine.

The mode of formation of flavanthrone in the alkali fusion of 2-aminoanthraquinone is discussed.

The 3 : 3′-di-*tert.*-butyl derivatives of indanthrone, indanthroneazine, and flavanthrone were prepared from *tert.*-butylbenzene. This was condensed with phthalic anhydride, and the product was nitrated, reduced, and cyclised to give 2-amino-3-*tert.*-butylanthraquinone amongst other products.

Many examples have been recorded of the effects of *o-tert.*-butyl substituents on the physical and chemical properties of organic compounds (Brown and Reagan, *J. Amer. Chem. Soc.*, 1947, **69**, 1032; Remington, *ibid.*, 1945, **67**, 1838; Brown and Cahn, *ibid.*, 1950, **72**, 2939). It was considered of interest, therefore, to prepare 3 : 3′-di-*tert.*-butylindanthrone (IX). Molecular models showed that neighbouring imino- and *tert.*-butyl groups approached sufficiently closely in this compound for the bulky alkyl groups to modify the properties of the dihydroazine nucleus.

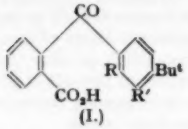
In preparing (IX) *o-p′-tert.*-butylbenzoylbenzoic acid (I; R = R′ = H) was obtained by Peters and Rowe's method (*J.*, 1945, 181) and then nitrated. Boiling nitric acid afforded a mixture of two isomeric mononitro-derivatives together with phthalic acid and *p-tert.*-butylnitrobenzene. A somewhat similar fission during nitration was observed by Legge (*J. Amer. Chem. Soc.*, 1947, **69**, 2086) who obtained *p-tert.*-butylnitrobenzene as a product of nitrating *p*-di-*tert.*-butylbenzene. The replacement of *p*-acyl by nitro-groups in the nitration of substituted amines and phenol ethers is not uncommon (Nightingale, *Chem. Reviews*, 1947, **40**, 117; van Romburgh, *Rec. Trav. chim.*, 1887, **6**, 367) but the analogous replacement of a *p*-acyl group in a derivative of *tert.*-butylbenzene has not been recorded previously. The result illustrates the marked electron-releasing character of the *tert.*-butyl group.

When a mixture of nitric and sulphuric acid was used in the nitration the formation of *p-tert.*-butylnitrobenzene was not observed. The product was almost wholly a mononitro-derivative, m. p. 203·5—204·5°. The same derivative and, in addition, an isomer, m. p. 187—188°, were formed by concentrated nitric acid alone. On reduction each nitro-derivative yielded the corresponding amine. That from the nitro-derivative of lower m. p. readily afforded a lactam. This was considered to have the structure (III), and hence the intermediate nitro- and amino-acids were *o*-(4-*tert.*-butyl-2-nitrobenzoyl)benzoic acid (II) and *o*-(2-amino-4-*tert.*-butylbenzoyl)benzoic acid (I; R = NH_2, R′ = H). The isomeric nitro-acid was considered to be *o*-(4-*tert.*-butyl-3-nitrobenzoyl)benzoic acid (IV), and the related amine *o*-(3-amino-4-*tert.*-butylbenzoyl)benzoic acid (I; R = H, R′ = NH_2). The last two structures are supported by the following considerations. Phthalic acid is not nitrated when it is heated with boiling nitric acid; this suggests that in the present instance nitration has been confined to the nucleus

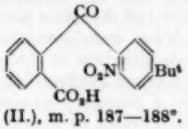
* Part IV, preceding paper.

carrying the *tert.*-butyl group. The amine (I; R = H, R′ = NH_2) can be diazotised and the resulting diazonium salt coupled to β-naphthol, but the diazonium salt is unusually unstable; in this respect it resembles the diazonium salt from *o-tert.*-butylaniline. The amine (I; R = NH_2, R′ = H) affords a diazonium salt having normal stability. In this it resembles *m-* and *p-tert.*-butylanilines (Shoesmith and Mackie, *J.*, 1928, 2334).

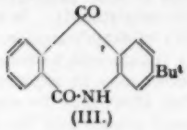
The cyclisation of (I; R = H, R′ = NH_2) to a derivative of anthraquinone occurred only with difficulty. Heating alone, or in a neutral solvent, or with phosphoric oxide, failed to bring



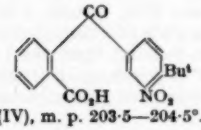
(I.)



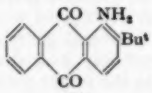
(II.), m. p. 187—188°.



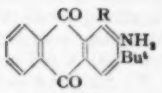
(III.)



(IV), m. p. 203·5—204·5°.



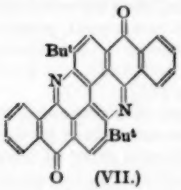
(V.)



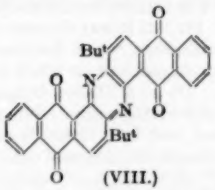
(VI.)

about ring closure. Heating with phosphorus pentachloride (cf. Scholl and Neovius, *Ber.*, 1911, **44**, 1075) gave an anthraquinone derivative in extremely small yield. The most practical method was to employ concentrated sulphuric acid. This reagent afforded 1-amino-2-*tert.*-butylanthraquinone (V) identical with Moualim and Peters's compound (*J.*, 1948, 1627) prepared by reducing 2-*tert.*-butyl-1-nitroanthraquinone. The result confirms the structures (IV) and (I; R = H, R′ = NH_2). In addition, 2-amino-3-*tert.*-butylanthraquinone (VI; R = H) was formed. The constitution of this compound rests on its composition, mode of derivation, and difference from (V). The yields of (V) and (VI; R = H) were 12% and 16%, respectively. A longer period of heating with sulphuric acid led to formation of 2-aminoanthraquinone in small amount.

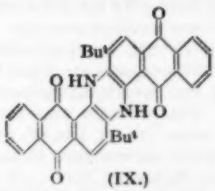
Although 2-aminoanthraquinone is easily brominated to form 2-amino-1 : 3-dibromoanthraquinone (Scholl, *Ber.*, 1907, **40**, 1700), yet 2-amino-3-*tert.*-butylanthraquinone forms a



(VII.)



(VIII.)



(IX.)

bromo-derivative with difficulty, when bromine is used as the brominating agent. The result was first considered to be a further illustration of the effect of an *o-tert.*-butyl substituent in restraining nuclear substitution. It is more probable, however, that the bromine substituent, once introduced, is easily eliminated in the presence of hydrogen bromide. By use of *N*-bromosuccinimide (Ziegler *et al.*, *Annalen*, 1942, **551**, 80) 2-amino-1-bromo-3-*tert.*-butylanthraquinone (VI; R = Br) was obtained in 57% yield.

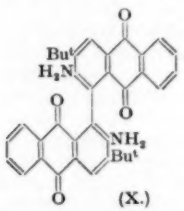
Heating 2-amino-3-*tert.*-butylanthraquinone with potassium hydroxide at 300° afforded 3 : 3′-di-*tert.*-butylflavanthrone (VII) in 65% yield. At 220° appreciable quantities of (VII) were again formed, but there was no indication of the presence of the related 3 : 3′-di-*tert.*-butylindanthrone (IX) or of the corresponding azine (VIII).

The result indicates that the 3-*tert.*-butyl substituent of 2-amino-3-*tert.*-butylanthraquinone prevents the formation of the indanthrone derivative or that this derivative is unstable, or finally that the formation of the flavanthrone is favoured. Several observations have been made which bear on these points.

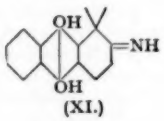
The dehydrogenation of 3 : 3′-di-*tert.*-butylindanthrone (IX) to the related azine (VIII) occurred quite readily, particularly in the presence of copper salts. Even on exposure to light, a solution of (IX) in chlorobenzene slowly became green. The change, azine (VIII) $\xrightarrow{+2H}$

dihydroazine (IX), occurred evidently on heating alone above 250°; it occurred also on heating with quinoline at the boiling point. 3 : 3′-Di-*tert.*-butylindanthrone is evidently less stable towards dehydrogenation than is indanthrone. Fieser and Fieser (*J. Amer. Chem. Soc.*, 1935, **57**, 491) have shown that the introduction of a methyl substituent into α-naphthaquinone enhances the stability of the quinone against reduction, and that carbonyl and halogen groups on the contrary stabilize the corresponding quinol against oxidation. Scholl (*Ber.*, 1903, **36**, 3410) recognized that the unusual stability of indanthrone, a dihydroazine, was dependent on the presence of four carbonyl groups, and that the stability could be enhanced by introducing halogen substituents. It would be expected therefore that alkyl substituents should reduce the stability of dihydroazines. In 3 : 3′-di-*tert.*-butylindanthrone the combined effect of two such groups is sufficient to make the dehydrogenation of (IX) to the azine (VIII) an easy process. The result may be explained by the marked electron-releasing character of *tert.*-alkyl groups, and this effect may be augmented by a tendency to overcome the interference between the *tert.*-butyl groups and the dihydroazine nucleus to which reference has been made.

In experiments designed to yield 3 : 3′-di-*tert.*-butylindanthrone (IX), 2-amino-1-bromo-3-*tert.*-butylanthraquinone (VI; R = Br) was heated with copper acetate and anhydrous sodium acetate in boiling *o*-dichlorobenzene. Several compounds were isolated from the product. These were : (*a*) A red compound, probably 2 : 2′-diamino-3 : 3′-di-*tert.*-butyl-1 : 1′-dianthraquinonyl (X), which passed rapidly into the bright yellow 3 : 3′-di-*tert.*-butylflavanthrone (VII)



(X.)



(XI.)

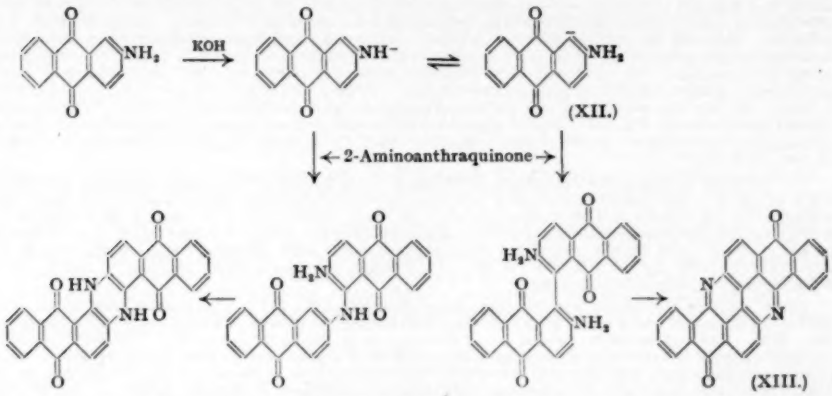
on contact with alkali or exposure to air. In this respect it resembled Scholl and Dischendorfer's red 2 : 2′-diamino-1 : 1′-dianthraquinonyl (*Ber.*, 1918, **51**, 452) which similarly easily yielded flavanthrone. (*b*) 3 : 3′-Di-*tert.*-butylflavanthrone (VII). The formation of a flavanthrone derivative by the self-condensation of a 2-amino-1-bromoanthraquinone has been reported only on one previous occasion. In D.R.-P. 172,733 it was claimed that flavanthrones result, possibly mixed with small quantities of indanthrones, when 2-amino-1 : 3-dibromo(or 1 : 3-dichloro)-anthraquinones are heated with a metallic salt and an alkali hydroxide or sodamide. (*c*) 3 : 3′-Di-*tert.*-butylindanthroneazine (VIII). (*d*) 3 : 3′-Di-*tert.*-butylindanthrone (IX).

The products were separated by chromatography. When the reaction had proceeded for 4 hours, (*a*), (*c*), and (*d*) were recognized, and from these (*b*) and additional amounts of (*c*) were formed on exposure to air. After 6 hours, (*b*), (*c*), and (*d*) were isolated, and after 24 hours only (*b*) and (*c*).

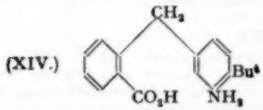
The introduction of two *tert.*-butyl groups into the molecules of indanthrone and flavanthrone causes other interesting changes in properties. Both 3 : 3′-di-*tert.*-butyl-indanthrone and -flavanthrone are much more soluble in organic solvents than are indanthrone and flavanthrone. The same effect of alkyl groups was reported by Bradley and Leete (*J.*, 1951, 2136) as the result of *N*-methylating indanthrone. The change in solubility was there ascribed to the effect of methylation in preventing the association of molecules of indanthrone, but the greater solubility of di-*tert.*-butylflavanthrone can only depend on a positive contribution by the *tert.*-butyl groups. 3 : 3′-Di-*tert.*-butylflavanthrone is less easily reduced than flavanthrone, a result which accords with Fieser and Fieser's work (*loc. cit.*) on the reduction of substituted α-naphthaquinones.

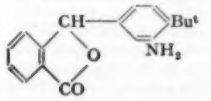
The formation of 3 : 3′-di-*tert.*-butylflavanthrone by the alkali fusion of 2-amino-3-*tert.*-butylanthraquinone at 220°, when 3 : 3′-di-*tert.*-butylindanthrone would be expected, raises the question how flavanthrones are formed by the alkali fusion of 2-aminoanthraquinones. Bohn's discovery of flavanthrone as a product of the alkali fusion of 2-aminoanthraquinone (D.R.-P. 133,686; Scholl, *Ber.*, 1907, **40**, 1691) was explained by Scholl (*loc. cit.*) as the result of the dehydrogenation of two molecules of 2-aminoanthraquinone to form 2 : 2′-diamino-1 : 1′-dianthraquinonyl. Schwenk (*Chem. Ztg.*, 1928, **52**, 45) held that 2-aminoanthraquinone and alkali yielded the radical (XI), which then polymerised to yield flavanthrone (XIII). An

acceptable view of the mechanism of the formation of flavanthrone from 2-aminoanthraquinone by the action of alkalis, however, must take account of the fact that indanthrone- and flavanthrone-formation are simultaneous reactions (Bohn, *loc. cit.*), and that for this reason they probably originate in the same primary process. Bradley and Leete (*loc. cit.*) have



suggested that the formation of indanthrone begins with the ionisation of 2-aminoanthraquinone, followed by the union of the anion with a second molecule of the amine. It appears probable that the formation of flavanthrone originates in the same process of ionisation, the anion reacting with the second molecule of 2-aminoanthraquinone in the form (XII). The formation of both a *C*- and an *N*-derivative by the reaction of the anion of 2-aminoanthraquinone with a molecule of 2-aminoanthraquinone is not unexpected (see Waters, " Physical Aspects of Organic Chemistry," Routledge and Kegan Paul Ltd., London, 4th Edition, p. 436). Alkylation of potassiopyrrole affords both *N*- and *C*-derivatives of pyrrole (Llubawin, *Ber.*, 1869, **2**, 101; Bell, *Ber.*, 1878, **11**, 1810; Ciamician and Dennstedt, *Ber.*, 1882, **15**, 2581; Ciamician and Silber, *Ber.*, 1887, **20**, 1369; Ciamician and Zanetti, *Ber.*, 1889, **22**, 659; Zanetti,


(XIV.)


(XV.)

ibid., p. 2518). Similarly, the sodio-derivative of indole when heated with methyl iodide affords 2- and 3-methylindole as well as *N*-methylindole (Weissgerber, *Ber.*, 1910, **43**, 3521).

At an early stage in the present work an attempt was made to obtain 2-amino-3-*tert.*-butylanthraquinone in better yield by first preparing the corresponding anthrone by cyclising the acid (XIV). Reduction of *o*-(3-amino-4-*tert.*-butylbenzoyl)benzoic acid (I; R = H, R′ = NH_2) by means of amalgamated zinc and hydrochloric acid gave the corresponding phthalide (XV), and this was almost unaffected when heated with zinc dust in aqueous sodium hydroxide (cf. Ullmann, *Annalen*, 1896, **291**, 17). Reduction of (I; R = H, R′ = NH_2) by ammonia, zinc dust, and copper sulphate (cf. Elbs, *J. pr. Chem.*, 1890, **41**, 121; Fieser and Newman, *J. Amer. Chem. Soc.*, 1936, **58**, 2376) afforded a product which contained much of the phthalide. Heating with hydrazine and the sodium salt of glycol yielded a phthalazine derivative (cf. Bergman and Pinchas, *J. Org. Chem.*, 1950, **15**, 1023).

Experimental.

Methyl o-p′-tert.-*Butylbenzoylbenzoate.*—*o-p′-tert.*-Butylbenzoylbenzoic acid was prepared by Peters and Rowe's method (*J.*, 1945, 181). Reaction was relatively slow; the yield of crude acid was 49% after 8 hours and 67% after 16 hours. Crystallisation from benzene–ligroin gave colourless plates, m. p. 152—153° (Peters and Rowe, *loc. cit.*, record m. p. 148—149°). The *methyl* ester, prepared by diazomethane, crystallised from methyl alcohol in large prisms, m. p. 69—70° (Found: C, 76·8; H, 6·7. $C_{19}H_{20}O_3$ requires C, 77·0; H, 6·8%). The same ester, m. p. 70—71° (Found: C, 76·9; H, 7·1%), was obtained in a yield of 0·5 g. when *o-p′-tert.*-butylbenzoylbenzoic acid (1 g.) was heated under reflux for

4 hours with concentrated hydrochloric acid (25 c.c.) and methyl alcohol (20 c.c.). There was no indication of the formation of *tert.*-butylbenzene in this preparation.

Nitration of o-p'-tert.-*Butylbenzoylbenzoic Acid.*—(*a*) The acid was unaffected by concentrated or fuming nitric acid in acetic acid at 100°.

(*b*) A mixture or concentrated nitric acid (7·3 c.c.) and concentrated sulphuric acid (75 c.c.) was added to a solution containing *o-p'-tert.*-butylbenzoylbenzoic acid (30 g.) in concentrated sulphuric acid (200 c.c.) at $\not>35°$. The solution was then kept for an hour and added to water. The precipitate was collected, dissolved in aqueous sodium carbonate (charcoal), and then recovered by acidification. A mononitration product, m. p. *ca.* 190°, obtained in almost quantitative yield, consisted almost entirely of the 3'-nitro-derivative. o-(4-tert.-*Butyl*-3-*nitrobenzoyl*)*benzoic acid* crystallises from toluene in small plates, m. p. 203·5—204·5°, softening at 195° (Found : C, 66·2; H, 5·2; N, 4·3. $C_{18}H_{17}O_5N$ requires C, 66·1; H, 5·2; N, 4·3%). It was recovered unaltered after being heated in boiling 5% aqueous sodium hydroxide for 5 hours. *Methyl* o-(4-tert.-*butyl*-3-*nitrobenzoyl*)*benzoate*, crystallised from methyl alcohol, had m. p. 129·5—130·5° (Found : C, 66·8; H, 5·6; N, 4·35. $C_{19}H_{19}O_5N$ requires C, 66·85; H, 5·6; N, 4·1%).

(*c*) When the nitration was carried out by adding 5 c.c. of fuming nitric acid to a solution containing 3·6 g. of *o-p'-tert.*-butylbenoylbenzoic acid in concentrated sulphuric acid (15 c.c.), and the product was heated at 95° for 2 hours, a tarry product slowly separated. There was no evidence of the formation of *p-tert.*-butylnitrobenzene (steam-distillation). Addition of ether caused the separation of a yellowish powder (1·25 g.), and this, recrystallised from aqueous acetic acid, afforded colourless needles, m. p. 240—241° (Found : C, 52·1; H, 4·0; N, 9·9. $C_{18}H_{16}O_9N_2$ requires C, 51·8; H, 3·6; N, 10·1%), of a 2-p-tert.-*butylbenzoyltrinitrobenzoic acid.*

(*d*) A solution containing *o-p'-tert.*-butylbenzoylbenzoic acid (20 g.) in concentrated nitric acid (100 c.c.) was heated under reflux for 30 minutes, then cooled and filtered; the residue (17·2 g.) had m. p. 165—175°. The mother-liquor yielded 4 g. of material, m. p. 165—175° (decomp.). The main fraction, crystallised from benzene and then from toluene, afforded *o*-(4-*tert.*-butyl-3-nitrobenzoyl)benzoic acid (7·3 g.), identical with that described under (*b*). The mother-liquors afforded 5·5 g. of material, m. p. 176—179°. After this had been separated and the liquor evaporated to dryness, an oil remained. The oil was mixed with dilute sodium carbonate solution and distilled in steam. The colourless distillate (*ca.* 2 c.c.) was heated for 3 hours with an excess of dilute acetic acid and iron filings (5 g.). The product was distilled in steam and the oily distillate was shaken with acetic anhydride; colourless crystals of *p-tert.*-butylacetanilide, m. p. 172—173°, separated. The m. p. was unchanged by authentic material (Legge, *J. Amer. Chem. Soc.*, 1947, **69**, 2086, records m. p. 174·6—175·2°). When the oily distillate was shaken with benzoyl chloride and an excess of dilute sodium hydroxide, *p-tert.*-butylbenzanilide separated having m. p. 142·5—143·5° not depressed by mixing with authentic material (Legge, *loc. cit.*, records m. p. 143·1—143·7°) (Found : C, 80·5; H, 7·2; N, 5·3. Calc. for $C_{17}H_{19}ON$: C, 80·6; H, 7·5; N, 5·5%).

The second fraction, m. p. 165—175° (decomp.), extracted with toluene, afforded a colourless residue (0·75 g.). This melted with decomposition at 197—200°, solidified immediately on cooling, and when reheated melted at 129°. Crystallisation from acetic acid afforded colourless prisms and these, sublimed *in vacuo*, gave phthalic anhydride, m. p. 130·5—131·5°. The toluene extract afforded a product on cooling. This, recrystallised several times from benzene, gave colourless plates of o-(4-tert.-*butyl*-2-*nitrobenzoyl*)*benzoic acid*, m. p. 187—188°, with previous sintering (Found : C, 66·4; H, 5·3; N, 4·25%). A mixture with the isomer, m. p. 203·5—204·5°, melted below 180°.

o-(3-*Amino*-4-tert.-*butylbenzoyl*)*benzoic Acid.*—A solution containing *o*-(4-*tert.*-butyl-3-nitrobenzoyl)-benzoic acid (6 g.) in aqueous ammonia (75 c.c.) was boiled for 15 minutes with ferrous hydroxide, prepared by adding aqueous ammonia (70 c.c.) to a solution of hydrated ferrous sulphate (40 g.) in water (300 c.c.). The resulting suspension was filtered, and the filtrate boiled to expel ammonia and then acidified with acetic acid. An oil separated and this solidified, forming a pale yellow powder (5·4 g.), m. p. 213—216° (decomp.). Repeated crystallisation from toluene afforded almost colourless leaflets of o-(3-*amino*-4-tert.-*butylbenzoyl*)*benzoic acid*, m. p. 218—219° (decomp.) (Found : C, 72·7; H, 6·5; N, 4·9. $C_{18}H_{19}O_3N$ requires C, 72·7; H, 6·4; N, 4·7%). Reduction of the nitro-acid by iron and acetic acid or sodium dithionite (hydrosulphite) in aqueous alkali or alcohol gave less satisfactory results.

The amino-acid could be diazotised below 0°; the diazonium salt coupled to alkaline β-naphthol to form an orange-red solution. Titration with standard sodium hydroxide indicated a molecular weight of 291 (Calc. for $C_{18}H_{19}O_3N$: *M*, 297). It was almost insoluble in concentrated hydrochloric acid, and no apparent change was caused by heating it with this reagent for 4 hours. It dissolved in 14% hydrochloric acid; after the solution had been boiled for 4 hours almost colourless needles separated. These consisted of the *hydrochloride* of o-(3-*amino*-4-tert.-*butylbenzoyl*)*benzoic acid* (Found : Cl^-, 9·4. $C_{18}H_{20}O_3NCl$ requires Cl^-, 10·6%). The hydrochloride softened at 200°, became red-brown, and finally decomposed without melting at 250°; it was soluble in cold 5% aqueous sodium carbonate (absence of lactam; cf. Kränzlein, *Ber.*, 1937, **70**, 1952). The product of thermal decomposition was insoluble in either hot 5% sodium hydroxide or hot 18% hydrochloric acid; a similar red-brown product resulted when the amino-acid was heated under reflux in *o*-dichlorobenzene for 40 minutes.

Methyl o-(3-*amino*-4-tert.-*butylbenzoyl*)*benzoate* was obtained as almost colourless prisms, m. p. 122—123° (Found : C, 73·3; H, 6·9; N, 4·2. $C_{19}H_{21}O_3N$ requires C, 73·3; H, 6·8; N, 4·5%), by esterifying the amino-acid with methanol and sulphuric acid. The identical product was obtained by reducing methyl *o*-(4-*tert.*-butyl-3-nitrobenzoyl)benzoate by iron and dilute acetic acid.

o-(2-*Amino*-4-tert.-*butylbenzoyl*)*benzoic acid* was prepared by reducing the 2'-nitro-acid with ammoniacal ferrous hydroxide. The filtrate afforded yellow crystals which decomposed at 130—140°. Dissolved in water and acidified, these yielded an acid which crystallised from benzene–ligroin in pale yellow plates, m. p. 176—177° (decomp.) (Found : C, 73·45; H, 6·2; N, 5·4%). The product consisted

essentially of *o*-(2-amino-4-*tert.*-butylbenzoyl)benzoic acid (yield, 50%). It diazotised readily; the diazonium salt afforded an orange solution when added to alkaline β-naphthol. Heated under reflux for 3 hours with 10 c.c. of 21% hydrochloric acid, the amino-acid (0·05 g.) gave, almost immediately, colourless, small plates (0·035 g.), which crystallised from aqueous alcohol in needles, m. p. 182·5—183·5° (Found: C, 76·45; H, 5·6; N, 4·8. $C_{18}H_{17}O_2N$ requires C, 77·4; H, 6·1; N, 5·0%). The composition of the product indicated that it was essentially the *lactam*.

3'-*Amino*-4'-tert.-*butylphenylphthalide*.—*o*-(3-Amino-4-*tert.*-butylbenzoyl)benzoic acid (1·4 g.), heated for 3 hours with amalgamated zinc (4 g.) and concentrated hydrochloric acid (25 c.c.), afforded an insoluble oil. Water was added, then sodium carbonate to neutrality; finally the suspension was extracted by means of ether. The evaporated extract afforded a brown solid (0·7 g.), and this was extracted by hot 5% aqueous sodium carbonate, and the residue crystallised from alcohol. Colourless crystals of the *phthalide* separated, having m. p. 139—140° (Found: C, 76·8; H, 7·0; N, 4·8. $C_{18}H_{19}O_2N$ requires C, 76·9; H, 6·8; N, 5·0%). This phthalide (m. p. 139—140°; 0·6 g.) also resulted when 2 g. of the amino-acid in 50 c.c. of dilute aqueous ammonia were heated under reflux for 56 hours with zinc dust (4 g.) and copper sulphate (0·5 g.), successive portions of ammonia being added every 2 hours. In this experiment the alkaline solution from which the phthalide had separated was filtered, acidified by means of acetic acid, and then extracted by means of ether. The extract yielded a tarry residue on evaporation; this was soluble in aqueous sodium carbonate. The filtered extract on acidification yielded 0·5 g. of a solid. Recrystallisation of this from benzene–ligroin afforded a small quantity of colourless needles, m. p. 115—116° (Found: C, 75·5; H, 6·9. $C_{18}H_{21}O_2N$ requires C, 76·3; H, 7·4%), which consisted essentially of o-(3-*amino*-4-tert.-*butylbenzyl*)*benzoic acid*. This *acid* dissolved in concentrated sulphuric acid with a yellow colour. When heated to 100° the solution became wine-red. According to Scholl and Neovius (*loc. cit.*), *o*-benzylbenzoic acid undergoes a similar change at 140°.

The phthalide was recovered unchanged after 4 hours' heating under reflux with zinc dust and 5% aqueous sodium hydroxide.

1-(3-*Amino*-4-tert.-*butylphenyl*)-4-*hydroxyphthalazine*.—*o*-(3-Amino-4-*tert.*-butylbenzoyl)benzoic acid (0·5 g.), heated with hydrazine under the conditions described by Huang-Minlon (*J. Amer. Chem. Soc.*, 1946, **68**, 2487), afforded 0·41 g. of an almost colourless powder, m. p. 278—280°. It was insoluble in aqueous sodium hydroxide or alcohol; it dissolved in concentrated hydrochloric acid. Crystallisation from toluene gave colourless platelets of the *phthalazine*, m. p. 278—280° (Found: C, 73·5; H, 6·2; N, 14·6. $C_{18}H_{18}ON_2$ requires C, 73·7; H, 6·5; N, 14·3%). Bergmann and Pinchas (*J. Org. Chem.*, 1950, **15**, 1023) have described an analogous product from 4-*o*-carboxybenzoyldiphenyl.

1-*Amino*-2-tert.-*butyl- and* 2-*Amino*-3-tert.-*butyl-anthraquinone*.—A solution containing *o*-(3-amino-4-*tert.*-butylbenzoyl)benzoic acid (5 g.) in concentrated sulphuric acid (50 c.c.) was heated at 155—160° for 10 minutes, then cooled and added to water. The dark brown precipitate (3·6 g.) was collected, washed, dried, and then extracted with benzene; there was a brown residue (1·3 g.). The solution was passed through a column of alumina. Several bands formed. The most mobile was orange-red; elution with benzene and recovery yielded a red powder (0·55 g.; m. p. 145—152°), which, recrystallised from aqueous acetic acid, gave red needles, m. p. 159—160°, not depressed on admixture with an authentic sample of 1-amino-2-*tert.*-butylanthraquinone, m. p. 160—161° (kindly provided by Dr. A. T. Peters), which had been prepared by the method of Moualim and Peters (*J.*, 1948, 1627).

The second, orange band was eluted by acetone. The extract was concentrated and then ligroin was added. On cooling, 0·74 g. of orange-yellow needles separated, having m. p. 203—205°. Recrystallisation from benzene gave pure 2-*amino*-3-tert.-*butylanthraquinone*, m. p. 205—205·5° (Found: C, 77·0; H, 6·2; N, 4·9. $C_{18}H_{17}O_2N$ requires C, 77·4; H, 6·1; N, 5·0%).

The chromatogram showed several fainter zones; there was also a strongly adsorbed dark red-brown band. When the time occupied by the ring closure was 20 minutes, a second and less mobile orange band appeared on the column. Elution by acetone and evaporation of the extract gave orange needles, m. p. 309—310°. Heating with acetic anhydride transformed these into yellow plates, m. p. 266—267°, not depressed on admixture with authentic 2-acetamidoanthraquinone.

o-(3-Amino-4-*tert.*-butylbenzoyl)benzoic acid was recovered almost unaltered after 2 hours' heating with concentrated sulphuric acid or 10% oleum at 95°, or after being dissolved in 20% oleum and kept at room temperature for 12 hours. Heating alone at 230° for 7 minutes, or with 75% sulphuric acid at 200°, or with phosphoric oxide in chlorobenzene gave none of the desired product. A small yield was obtained by heating the amino-acid with phosphorus pentachloride in boiling chlorobenzene for 3 hours.

2-Amino-3-*tert.*-butylanthraquinone formed a yellow solution in sulphuric acid. Alkaline sodium dithionite dissolved it, forming a red solution. Its orange solution in pyridine became reddish-brown on addition of methyl-alcoholic potassium hydroxide; the original colour was regenerated on addition of methanol. It formed a yellow solution in acetic anhydride and this became colourless when heated with boroacetic anhydride. There was no indication of the formation of a flavanthrone derivative when 2-amino-3-*tert.*-butylanthraquinone was heated with antimony pentachloride in nitrobenzene. The absorption spectrum of a solution in benzene was closely similar to that of 2-aminoanthraquinone in the same solvent.

1-Amino-2-*tert.*-butylanthraquinone formed orange solutions in both sulphuric acid and alkaline sodium dithionite. Addition of boroacetic anhydride to its orange solution in acetic anhydride caused a change in colour to bluish-red; the solution showed a strong red-violet fluorescence in ultra-violet light. The orange solution in pyridine was unchanged on addition of methyl-alcoholic potassium hydroxide. Heating for 2 hours at 100° with benzoyl chloride containing a few drops of concentrated sulphuric acid afforded 1-*benzamido*-2-tert.-*butylanthraquinone*, which crystallised from dilute acetic acid in yellow needles, m. p. 250—250·5° (Found: C, 77·5; H, 5·5; N, 3·8. $C_{25}H_{21}O_3N$ requires C, 78·3; H, 5·5; N, 3·7%). A solution in benzene showed maximum light absorption at 4800 Å; a similar solution of 1-aminoanthraquinone showed a maximum at 4650 Å.

2-Amino-1-bromo-3-tert.-butylanthraquinone.—A solution containing 2-amino-3-*tert.*-butylanthraquinone (0·48 g.) in carbon tetrachloride (50 c.c.) was heated under reflux for 5 hours with *N*-bromosuccinimide (0·31 g.), then cooled, and the precipitated succinimide (0·15 g.) collected (cf. Ziegler *et al.*, *Annalen*, 1942, **551**, 80). The filtrate was concentrated and then chromatographed on a column of alumina; two main bands formed. On development with benzene the faster orange-yellow band passed through the column, and evaporation of the eluate afforded small plates (0·35 g.), m. p. 211—215°. Recrystallisation from benzene–ligroin gave orange-yellow needles, m. p. 212—215° (Found: C, 60·3; H, 4·6; N, 3·6; Br, 22·0. $C_{18}H_{16}O_2NBr$ requires C, 60·3; H, 4·5; N, 3·9; Br, 22·35%). *2-Amino-1-bromo-3-tert.-butylanthraquinone* forms yellow solutions in concentrated sulphuric acid and pyridine. A green colour develops when methyl-alcoholic potassium hydroxide is added to the pyridine solution. The quinone dissolves in alkaline sodium dithionite with a red colour.

The second band was reddish-orange; it yielded a small quantity of unchanged 2-amino-3-*tert.*-butylanthraquinone.

When bromine was added to a solution of 2-amino-3-*tert.*-butylanthraquinone in acetic acid yellow crystals separated. The product had m. p. 240—244°. It could not be obtained pure by recrystallisation; when its solution in acetic acid was added to water, 2-amino-3-*tert.*-butylanthraquinone was regenerated. The amine was also recovered mainly unaltered when it was heated at 160—170° in solution in nitrobenzene with an excess of bromine and much anhydrous sodium acetate.

Action of Fused Potassium Hydroxide on 2-Amino-3-tert.-butylanthraquinone. Formation of 3 : 3′-Di-tert.-butylflavanthrone.—2-Amino-3-*tert.*-butylanthraquinone (0·2 g.) was added to molten potassium hydroxide (5 g.) at 295—305°. After 20 minutes at this temperature the melt had become dark and a small amount of the amine had sublimed. The product was cooled, added to water (50 c.c.), and aerated for an hour. The yellowish-brown precipitate (0·12 g.) was collected, washed, dissolved in *o*-dichlorobenzene, and chromatographed on alumina. A strongly adsorbed brown zone formed, and a more mobile intensely yellow band. The latter passed through the column on development with benzene. The resulting eluate gave a product which crystallised from *o*-dichlorobenzene–methanol in small, brownish-yellow needles (Found: C, 82·9; H, 5·7; N, 5·1. $C_{36}H_{28}O_2N_2$ requires C, 83·1; H, 5·4; N, 5·4%). **3 : 3′-Di-tert.-butylflavanthrone** is much more soluble in organic solvents than is flavanthrone; even in the cold, it dissolves in benzene, forming a solution which is distinctly yellow. In concentrated sulphuric acid it gives a bright orange solution. The yellow solution in hot pyridine becomes green on addition of methyl-alcoholic potassium hydroxide; excess of the reagent changes the colour to yellow and finally yields a precipitate. Flavanthrone behaves similarly, the yellow solution in pyridine becoming blue on addition of methyl-alcoholic potassium hydroxide; excess of the reagent gives a bluish-red precipitate. Like flavanthrone, 3 : 3′-di-*tert.*-butylflavanthrone gives a blue colour with cold 30—40% oleum, and on heating a red-violet. Scholl (*Ber.*, 1907, **40**, 1691) recorded that flavanthrone gave a red-violet colour with cold oleum, and on heating a blue. 3 : 3′-Di-*tert.*-butylflavanthrone dissolves in piperidine, forming a yellow solution; addition of hydrazine causes development of a blue colour and a red fluorescence. 3 : 3′-Di-*tert.*-butylflavanthrone dissolves in alkaline sodium dithionite, forming a blue solution; in reflected artificial light the solution exhibits a characteristic, intense violet colour; aeration re-forms the original orange-yellow colouring matter. The substance differs from flavanthrone in not being reduced by aqueous sodium sulphide.

When the potassium hydroxide fusion was carried out at 215—225° the product was more complex. Unchanged amine (15%) was recovered, the proportion of acidic compounds was higher than at 295—300°, and 3 : 3′-di-*tert.*-butylflavanthrone was isolated in appreciable amount, but there was no indication of the formation of a blue indanthrone derivative or the corresponding azine.

Self-condensation of 2-Amino-1-bromo-3-tert.-butylanthraquinone. Formation of 3 : 3′-Di-tert.-butylflavanthrone, -indanthrone, and -indanthroneazine.—(*a*) A solution containing 0·15 g. of 2-amino-1-bromo-3-*tert.*-butylanthraquinone in 5 c.c. of *o*-dichlorobenzene was heated under reflux for 24 hours with finely powdered sodium acetate (0·5 g.) and a trace of copper acetate. The solution, initially yellow, became green and then brown. The cooled suspension was filtered, and the residue washed in turn with benzene, alcohol, and water. The resulting dark powder (0·03 g.) had a yellowish-green lustre. It was chromatographed in chlorobenzene on alumina; two bands were formed. The lower, orange-yellow band consisted of 3 : 3′-di-*tert.*-butylflavanthrone, identical with the same compound prepared by the alkali fusion of 2-amino-3-*tert.*-butylanthraquinone. The more strongly adsorbed band was greenish-yellow, it consisted of 3 : 3′-di-*tert.*-butylindanthrone azine [see Experiment (*b*)].

The *o*-dichlorobenzene filtrate, passed through an alumina column, yielded a number of faint bands, and in addition an intense yellow band consisting of 3 : 3′-di-*tert.*-butylflavanthrone.

(*b*) In a similar experiment the heating was stopped after 6 hours; the suspension was then deep green. The undissolved material was collected and treated as in (*a*); it yielded 0·062 g. of a dark green microcrystalline powder. This product was chromatographed in chlorobenzene on alumina. Two main zones were formed, the upper zone blue and the lower zone yellow. Developed by means of benzene the blue zone separated into two closely similar bands. Elution of the yellow band yielded a dark, yellowish-green powder (0·022 g.) consisting of 3 : 3′-*di*-tert.-*butylindanthroneazine* (Found: C, 77·5; H, 5·4; N, 4·6. $C_{72}H_{52}O_4N_4$ requires C, 78·3; H, 5·1; N, 5·1). The azine dissolved in concentrated sulphuric acid with a red-brown colour. It gave the same colour in contact with 30—40% oleum. It dissolved in pyridine with a yellow colour, changed to green by addition of methyl-alcoholic potassium hydroxide. It dissolved with difficulty in alkaline sodium dithionite forming a blue solution; aeration gave a blue precipitate consisting of 3 : 3′-di-*tert.*-butylindanthrone (difference from 3 : 3′-di-*tert.*-butylflavanthrone).

Heated in air, the azine became green and then blue. When cooled at the point of melting, it yielded a dark product which exhibited a reddish metallic glance. This product dissolved in cold *o*-dichlorobenzene with a blue colour; in concentrated sulphuric acid the solution was red. The azine dissolved in

quinoline with a blue-green colour, in aniline with a green, and in piperidine with a greenish-blue colour, changed to blue on addition of hydrazine hydrate.

The two blue bands were eluted together by means of methanol–chlorobenzene. Evaporation yielded 0·013 g. of dark blue leaflets consisting of impure 3 : 3′-di-*tert.*-butylindanthrone (Found : C, 75·6; H, 5·4; N, 6·7%). These dissolved in cold benzene, forming a pale blue solution. The solution in chlorobenzene showed maximum absorption at 7250 Å; on exposure to light it became progressively greener. After several weeks the absorption spectrum had changed considerably, absorption had become very strong in the red region, the absorption maximum had moved to 6900 Å., the intensity at the maximum had diminished, and absorption had become noticeable in the blue. In concentrated sulphuric acid there was maximum absorption at 4700 Å ($E = 148$); the absorption decreased and then increased again at longer wave-lengths, ε being 0·64 at 7000 Å. Addition of a drop of nitric acid to the solution in sulphuric acid changed the colour to yellow-brown immediately. The dihydroazine dissolved with difficulty in alkaline sodium dithionite, forming a blue solution. Aeration afforded a greenish-blue precipitate. As with many difficulty reducible quinones, the process of dissolving it in an alkaline reducing medium was facilitated by addition of pyridine (cf. Bradley and Sutcliffe, *J.*, in the press). It gave a greenish-olive colour with 30—40% oleum, changed (irreversibly) to red-brown on heating.

(*c*) In a third experiment the heating was stopped after 4 hours. The green solution was passed through a column of alumina whilst it was still warm, and without previous filtration. Development by chlorobenzene gave several bands; the most mobile was yellow, and this was succeeded by a bright red, a deep blue, and a deep brown zone. As development proceeded, increasing amounts of a yellow eluate were collected, whilst the remaining bands moved slowly down the column. It was then found that the yellow zone was being formed on the column from the blue. The yellow eluate afforded 0·043 g. of 3 : 3′-di-*tert.*-butylindanthroneazine. Exposure to light caused the yellow azine to become progressively greener.

The bright red band became bright yellow as soon as it was brought into contact with aqueous sodium hydroxide or exposed to air. For this reason the properties of the red compound could not be studied in detail. The yellow product was identified as 3 : 3′-di-*tert.*-butylflavanthrone; the yield was 0·01 g.

The authors thank the University of Leeds for the award of a Bradford Dyers' Association Research Fellowship to one of them (H. E. N.).

CLOTHWORKERS RESEARCH LABORATORY,
THE UNIVERSITY, LEEDS.

[*Received, April 20th*, 1951.]

---

475. *Chemistry of Indanthrone. Part VI.* Alkylsulphonylindanthrones.*

By WILLIAM BRADLEY and HARRY E. NURSTEN.

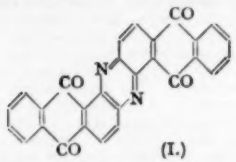
Consideration of the influence of carbonyl and halogen substituents in stabilising indanthrone against dehydrogenation (Scholl, *Ber.*, 1903, **36**, 3410), and of toluenesulphonyl groups in facilitating the reduction of α-naphthaquinone (Fieser and Fieser, *J. Amer. Chem. Soc.*, 1935, **57**, 491) has led to an investigation of the influence of alkylsulphonyl substituents on the stability of indanthrone. It has been found that alkylsulphonyl substituents are more effective than chlorine substituents similarly placed. The 3-alkylsulphonyl substituent has a marked effect in augmenting the acid properties of indanthrone and this is considered to be the reason for the greater stability of alkylsulphonylindanthrones towards dehydrogenation.

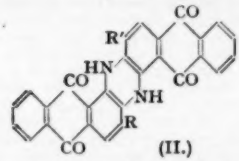
In preparing the indanthrone derivatives, 2-(4-chloro-3-nitrobenzoyl)-benzoic acid was caused to react with alkanethiols, and the resulting 4′-alkylthio-acids were oxidised to the related 4′-alkylsulphonyl-acids. These were reduced, and the derived amines were cyclised to give mainly the 3-alkylsulphonyl-2-aminoanthraquinones. The 3-ethylsulphonyl and 3-butylsulphonyl compounds were brominated, and the 1-bromo-derivatives so obtained were condensed to give the corresponding 3 : 3′-dialkylsulphonylindanthrones.

MANY researches have combined to show that azines are usually more stable than the related dihydroazines. *NN*-Dihydrophenazine, readily formed by reducing phenazine, is easily dehydrogenated merely by heat (Claus, *Annalen*, 1873, **168**, 1), and the eurhodines, though easily reduced, are re-formed by exposing their dihydro-forms to air.

* Part V, preceding paper.

In the indanthrone series the dihydroazine is more stable than the azine. Simple heating of indanthroneazine (I) with phenol, quinoline, or even nitrobenzene brings about reduction to indanthrone (II; R = R′ = H). Scholl (*Ber.*, 1903, **36**, 3410) recognized that the stability of indanthrone was dependent on the presence of four carbonyl groups, and he showed that the stability was augmented by halogen substituents and diminished by amino- and anilino-groups.

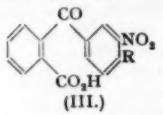

(I.)

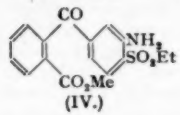

(II.)

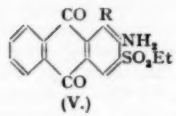
Fieser and Fieser (*J. Amer. Chem. Soc.*, 1935, **57**, 491) studied the effect of substituents on the ease of reduction of α-naphthaquinone. Like Scholl, they found that carbonyl and halogen substituents stabilized the dihydro-form, whilst amino- and substituted amino-groups stabilised the quinone. In an extensive series of experiments they (*loc. cit.*) observed that the toluenesulphonyl group exerted by far the greatest effect in stabilising the dihydro-form. For this reason it was of interest to prepare a number of 3 : 3′-dialkylsulphonylindanthrones (II; R = R′ = SO_2Alk) with the object of observing whether alkylsulphonyl substituents are equally able to increase the stability of indanthrone against dehydrogenation to the azine form.

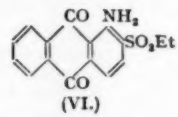
In one example, 3 : 3′-diethylsulphonylindanthrone (II; R = R′ = SO_2Et) was prepared by the following means. 2-*p*-Chlorobenzoylbenzoic acid was nitrated and the *m*-nitro-derivative (III; R = Cl) reacted with ethanethiol to form 2-(4-ethylthio-3-nitrobenzoyl)-benzoic acid (III; R = SEt). Oxidation afforded the sulphone (III; R = SO_2Et) and subsequent reduction of the methyl ester gave methyl 2-(3-amino-4-ethylsulphonylbenzoyl)-benzoate (IV). This compound or the related free acid cyclised to form a mixture of 2-amino-3-ethylsulphonyl- (V; R = H) and 1-amino-2-ethylsulphonyl-anthraquinone (VI). The former was isolated and brominated, and the 2-amino-1-bromo-3-ethylsulphonylanthraquinone (V; R = Br) so obtained was condensed by known methods to give 3 : 3′-diethylsulphonyl-indanthrone.

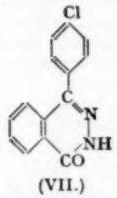
2-(4-Chloro-3-nitrobenzoyl)benzoic acid in contact with alkaline reagents readily yielded the hydrate of 2-(4-hydroxy-3-nitrobenzoyl)benzoic acid (III; R = OH). 2-Amino-1-bromo-3-ethylsulphonylanthraquinone yielded a diacetyl derivative; when it was heated with benzoyl chloride in pyridine the oxazole (IX) resulted.

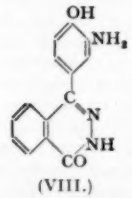

(III.)

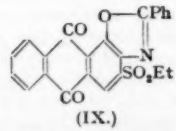

(IV.)


(V.)


(VI.)


(VII.)


(VIII.)


(IX.)

In a parallel series of preparations 2-(4-chloro-3-nitrobenzoyl)benzoic acid was converted into 3 : 3′-dibutylsulphonylindanthrone (II; R = R′ = SO_2Bu).

In a third series of preparations 2-amino-3-*iso*propylsulphonylanthraquinone was prepared from 2-(4-chloro-3-nitrobenzoyl)benzoic acid, but the amount obtained was insufficient to enable 3 : 3′-di*iso*propylsulphonylindanthrone to be prepared.

Methyl 2-(4-ethylsulphonyl-3-nitrobenzoyl)benzoate, heated with dilute aqueous sodium hydroxide, readily yielded the hydrate of 2-(4-hydroxy-3-nitrobenzoyl)benzoic acid (III; R = OH), the ethylsulphonyl group having been replaced by hydroxyl. A similar instance of the ready replacement of a sulphone substituent was recorded by Levi and Smiles (*J.*, 1932,

1488) who obtained *o*-nitrodiphenylamine from 2-nitrodiphenyl sulphone and aniline, *o*-nitrophenyl *p*-tolyl ether from the same sulphone and sodium *p*-tolyl oxide, and *o*-nitrophenol from 4-hydroxy-2′-nitrodiphenyl sulphone and aqueous sodium hydroxide.

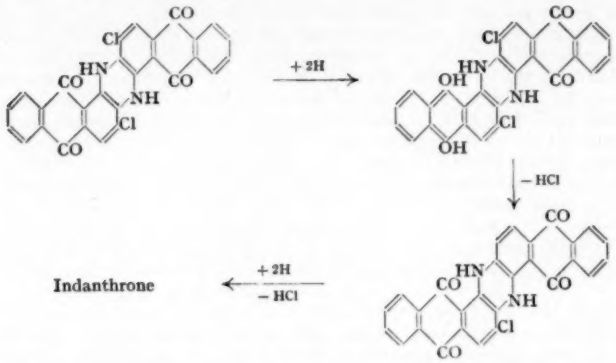
It was not found possible to cyclise the 2-(4-ethylsulphonyl-3-nitrobenzoyl)benzoic acid to the related anthraquinones, a circumstance which accords with earlier experience with nitrobenzoylbenzoic acids (Hofmann, *Monatsh.*, 1915, **36**, 805). Heating with concentrated sulphuric acid sufficed to cyclise the related 2-(3-amino-4-alkylsulphonylbenzoyl)benzoic acids. In each instance the main product was the desired 3-alkylsulphonyl-2-aminoanthraquinone, but the isomeric 2-alkylsulphonyl-1-aminoanthraquinone was formed in small amount in all cases. The isomers were readily separable by crystallisation and chromatography, the α-amino-compounds being the less readily retained on the alumina column. In contrast with 2-amino-anthraquinone which can be brominated with great ease (D.R.-P. 158,474; Scholl, *Ber.*, 1907, **40**, 1700) both 2-amino-3-ethyl- and 2-amino-3-butyl-sulphonylanthraquinone are brominated only with difficulty. The result is not unexpected (cf. Baldwin and Robinson, *J.*, 1932, 1445). Both amino-sulphones show acidic properties; a change in colour occurs when methyl-alcoholic potassium hydroxide is added to their solutions in pyridine (Bradley and Leete, *J.*, 1951, 2132). Like Scholl (*loc. cit.*), who observed 2-amino-1 : 3-dibromoanthraquinone to form a *NN*-diacetyl derivative with ease, we obtained a *NN*-diacetyl derivative when 2-amino-1-bromo-3-ethylsulphonylanthraquinone was heated with a mixture of acetyl chloride and acetic anhydride; the amine was unaffected when heated with acetic anhydride or benzoyl chloride containing a small proportion of concentrated sulphuric acid (cf. also Sudborough, *Proc.*, 1901, **17**, 45).

The 3 : 3′-dialkylsulphonylindanthrones were prepared from the corresponding 3-alkyl-sulphonyl-2-amino-1-bromoanthraquinones by the method of D.R.-P. 158,287. The yield was 40% with the 3-ethylsulphonyl and 32% with the 3-butylsulphonyl derivative. The latter was much more soluble in organic solvents than the former, which itself was more soluble than indanthrone. This effect of alkyl groups has also been observed with the *N*-methyl- and *NN*-dimethyl-indanthrones (Bradley and Leete, *J.*, 1951, 2136). The absorption spectra of the alkylsulphonylindanthrones in α-chloronaphthalene resemble those of 3 : 3′-dichloro- and 3 : 3′-dibromo-indanthrones in the same solvent and also those of *N*-methyl- and *NN*-dimethyl-indanthrones in *o*-dichlorobenzene (*idem*, *ibid.*) (see table). Although they absorb mainly at shorter wave-lengths, solutions of the two sulphonyl derivatives appear greener than those of the halogen compounds.

Indanthrone substituent.	Absorption max. (Å): (*a*) main band.	(*b*) subsidiary band.	Intensity ratio, (*a*)/(*b*)
N-Methyl	6650	—	—
NN-Dimethyl	6550	6200?	1·09
3 : 3′-Diethylsulphonyl	7050	6525	1·36
3 : 3′-Dibutylsulphonyl	7050	6550	1·34
3 : 3′-Dichloro	7200	6625	1·19
3 : 3′-Dibromo	7225	6650	1·22

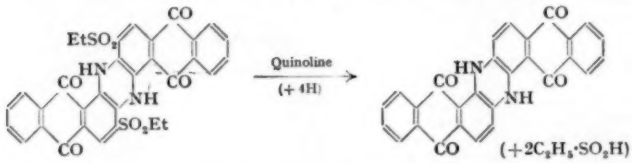
The two dialkylsulphonylindanthrones show interesting chemical properties. 3 : 3′-Diethylsulphonylindanthrone, which was studied in greater detail, proved to be less readily dehydrogenated by alkali hypochlorites than was 3 : 3′-dichloroindanthrone. The result accords with Scholl's observation (*Ber.*, 1903, **36**, 3410) relating the electrical character of substituents to their effect on the stability of indanthrone and with the recognition by Fieser and Fieser (*loc. cit.*) that the toluenesulphonyl substituent stabilises 1 : 4-dihydroxynaphthalene towards dehydrogenation to α-naphthaquinone more effectively than chlorine or bromine. Both 3 : 3′-diethylsulphonylindanthrone and the homologous 3 : 3′-dibutylsulphonyl compound are relatively strong acids which yield green salts when methanolic potassium hydroxide is added to their solutions in pyridine. Since the oxidation of a dihydroazine to an azine requires the removal of two hydrogen atoms each with one electron, the increase in acid strength is related in a simple manner to the increased stability towards oxidation, because it involves an increased tendency of the hydrogens to separate as protons. Both derivatives were reduced by aqueous sodium hydroxide containing sodium dithionite (hydrosulphite); the ethyl derivative was sparingly soluble, giving a green solution, but the butyl compound was almost insoluble. These colouring matters were largely unaltered by reduction followed by oxidation. In contrast, 3 : 3′-dichloroindanthrone, which is much more soluble in alkaline sodium dithionite,

lost much of its halogen, presumably because of the greater stability of chlorine as an anion and the occurrence of the reaction :

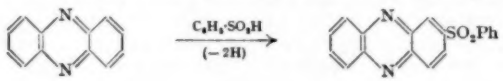


A number of publications have referred to the ease of replacement of halogens in 3 : 3′-dihalogenoindanthrones. U.S.P. 1,634,473 mentions the formation of indanthrone when 3 : 3′-dibromoindanthrone is heated with alcoholic potassium hydroxide. Halogen is also replaced by hydrogen when halogenated indanthrones are heated with aromatic amines in the presence of copper compounds (U.S.P. 1,790,887). Several U.S. patents (1,862,843—5, 2,377,158, and 2,413,483) refer to the replacement of bromine by chlorine in 3 : 3′-dibromoindanthrone. In the present experiments 3 : 3′-dibromoindanthrone was not affected by boiling dibutylamine, dimethylaniline, or 20% aqueous potassium hydroxide. It was also unaffected when heated with dry piperidine at the boiling point. When a small proportion of water was present 40% of the bromine was replaced in 9 hours.

3 : 3′-Diethylsulphonylindanthrone, heated with quinoline or dry piperidine, afforded indanthrone. It appears that the colouring matter loses the elements of ethylsulphinic acid



and that the resulting azine is then reduced. The reaction provides an illustration of the reversal of the reaction described by Hinsberg and Himmelschein (*Ber.*, 1896, **29**, 2020) in which benzenesulphinic acid reacts with phenazine to form 2-phenylsulphonylphenazine.



Experimental.

2-(4-*Ethylthio*-3-*nitrobenzoyl*)*benzoic Acid.*—2-*p*-Chlorobenzoylbenzoic acid, nitrated with 97% nitric acid at 25—30°, gave 2-(4-chloro-3-nitrobenzoyl)benzoic acid, m. p. 200·5—201°, in 85% yield. According to D.R.-P. 148,110, the nitro-acid melts at 202—204° (cf. B.I.O.S. Final Report No. 987, p. 13). Ethanethiol (2·65 c.c.) was dissolved in a solution of sodium ethoxide prepared from sodium (1·5 g.) and absolute alcohol (100 c.c.). The solution was added to one of the nitro-acid (10 g.) in alcohol (100 c.c.), and the mixture was heated for 2 hours under reflux, then poured into water and acidified. The oil which separated soon solidified (10·6 g.); the *acid* then crystallised from methanol in yellow plates, m. p. 173° (Found : C, 58·0; H, 3·9; N, 4·0; S, 9·2. $C_{16}H_{13}O_5NS$ requires C, 58·0; H, 3·9; N, 4·2; S, 9·7%). Preparations on a larger scale gave lower percentage yields. The same compound resulted when aqueous sodium hydroxide was substituted for the alcoholic sodium ethoxide, but products of higher m. p. were also formed. The *methyl* ester crystallised from methanol in pale yellow needles, m. p. 124·5—125·5° (Found : N, 3·9; S, 8·8. $C_{17}H_{15}O_5NS$ requires N, 4·1; S, 9·3%). The *ethyl* ester

separated from methanol in yellow prisms, m. p. 88—90° (Found: N, 3·7; S, 8·8. $C_{16}H_{17}O_5NS$ requires N, 3·9; S, 8·9%).

2-(4-*Ethylsulphonyl*-3-*nitrobenzoyl*)*benzoic Acid*.—Hydrogen peroxide (4 c.c.; 100-vol.) was added to a solution of 2-(4-ethylthio-3-nitrobenzoyl)benzoic acid (3 g.) in acetic acid (50 c.c.), and the mixture was then heated on the steam-bath for 4 hours until colourless. It was concentrated and cooled, and the crystalline product was collected (m. p. 128—129°, unaltered by recrystallisation from acetic acid). Further successive recrystallisation from chlorobenzene, *o*-dichlorobenzene, and finally from benzene–ligroin afforded the *acid* as colourless, small needles, m. p. 158° after sintering at 155° (Found: C, 52·9; H, 3·6; N, 4·4; S, 9·6. $C_{16}H_{15}O_7NS$ requires C, 52·9; H, 3·6; N, 3·9; S, 8·8%). This acid did not undergo ring-closure when heated with 20% oleum at 100° for 7 hours.

Oxidation of the ethylthio-acid to the ethylsulphonyl-acid also occurred when chromium trioxide in acetic acid was employed as oxidant, but the results were inferior to those obtained as above. Potassium permanganate in acetic acid proved unsatisfactory, as also did the use of fuming nitric acid.

Methyl 2-(4-*ethylsulphonyl*-3-*nitrobenzoyl*)*benzoate* was prepared in 80% yield by heating the corresponding crude acid, m. p. 128—129°, with methyl alcohol and sulphuric acid. It crystallised from methyl alcohol in almost colourless, rectangular plates, m. p. 127—128° (Found: C, 54·0; H, 3·9; N, 4·0; S, 9·0. $C_{17}H_{15}O_7NS$ requires C, 54·1; H, 4·0; N, 3·7; S, 8·5%). It was also prepared by oxidising methyl 2-(4-ethylthio-3-nitrobenzoyl)benzoate by means of hydrogen peroxide. The *ethyl* ester separated from ether in the form of a colourless, crystalline mass, m. p. 110—111° (Found: C, 55·3; H, 4·3; N, 3·8; S, 8·4. $C_{18}H_{17}O_7NS$ requires C, 55·25; H, 4·3; N, 3·6; S, 8·2%).

2-(4-*Hydroxy*-3-*nitrobenzoyl*)*benzoic Acid*.—(*a*) A solution containing 2-(4-chloro-3-nitrobenzoyl)-benzoic acid (3 g.) in 5% aqueous sodium hydroxide (100 c.c.) was heated under reflux for an hour and then acidified. Pale yellow plates (2·7 g.), m. p. 150—161° (decomp.), separated. Repeated crystallisation from methyl alcohol and then aqueous acetic acid gradually raised the m. p. of the *hydrate* to 180—180·5°, with previous softening (Found: C, 54·9; H, 3·6; N, 4·3. $C_{14}H_9O_6N,H_2O$ requires C, 55·1; H, 3·6; N, 4·6%). Thiel and Diehl (*Chem. Zentr.*, 1927, II, 2669) record m. p. 180—181°; U.S.P. 1,654,287 gives m. p. 175°; B.I.O.S. Final Report No. 987, p. 14 and F.I.A.T. Final Report No. 1313, p. 154 give m. p. 165—167°, but none of these appears to have recognized that the acid is a monohydrate. Titration against sodium hydroxide (phenolphthalein) gave *M*, 306, the acid being assumed to be dibasic ($C_{14}H_9O_6N,H_2O$ requires *M*, 305). There was no indication of pseudo-acid properties. Heated at 160°/0·5 mm., the acid yielded a sublimate consisting of rosettes of pale yellow rods of a *hemihydrate*, m. p. 179—180° (Found: C, 56·6; H, 3·6. $C_{14}H_9O_6N,0·5H_2O$ requires C, 56·8; H, 3·35%). The *methyl* ester crystallised from methyl alcohol in pale yellow, rectangular plates, m. p. 148—149° (Found: C, 59·3; H, 3·8; N, 4·5. $C_{16}H_{11}O_6N$ requires C, 59·8; H, 3·7; N, 4·7%).

(*b*) Methyl 2-(4-ethylsulphonyl-3-nitrobenzoyl)benzbate (3 g.) was heated under reflux for 30 minutes with 5% aqueous sodium hydroxide (100 c.c.). The acidified product afforded 2·0 g. of golden-yellow plates, m. p. 158—160° (decomp.). Recrystallisation raised the m. p. to 179·5—180°, not depressed by admixture with the acid prepared as described under (*a*) (Found: C, 55·2; H, 3·8; N, 4·2%).

2-(4-*Acetoxy*-3-*nitrobenzoyl*)*benzoic acid*, obtained by heating the hydroxy-acid with acetic anhydride, crystallised from aqueous acetic acid in colourless plates, m. p. 177—179° (Found: N, 4·2. $C_{16}H_{11}O_7N$ requires N, 4·0%).

1-(3-*Amino*-4-*hydroxyphenyl*)-4-*hydroxyphthalazine*.—Heated under reflux for 2 hours with 100% hydrazine hydrate, 2-(4-hydroxy-3-nitrobenzoyl)benzoic acid dissolved, forming a deep orange-red solution which later became yellow. Almost colourless needles separated; these darkened at 275°, began to decompose at 280°, and finally melted at 298—300° (Found: N, 16·5. $C_{14}H_{11}O_2N_3$ requires N, 16·6%). The *phthalazine* dissolved with a yellow colour in cold aqueous sodium hydroxide; it also dissolved in cold hydrochloric acid and in hot acetic acid, but was sparingly soluble in methyl alcohol and almost insoluble in toluene. It contained a diazotisable amino-group.

2-(4-Hydroxy-3-nitrobenzoyl)benzoic acid did not react with hydroxylamine in aqueous sodium hydroxide or with 2 : 4-dinitrophenylhydrazine in acetic acid.

2-(3-*Amino*-4-*ethylsulphonylbenzoyl*)*benzoic Acid*.—A solution containing 2-(4-ethylsulphonyl-3-nitrobenzoyl)benzoic acid (2·7 g.) and sodium dithionite (5 g.) in 1% aqueous sodium hydroxide (50 c.c.) was warmed slowly and then heated under reflux for an hour. The solution was cooled, acidified by acetic acid, and then extracted with ether. The extract was evaporated to dryness, and the residue crystallised from dilute acetic acid; a product (0·5 g.), m. p. 187—190°, was obtained. Recrystallisation from the same solvent gave almost colourless plates, m. p. 191—192° (Found: C, 57·5; H, 4·7; N, 4·2; S, 9·1. $C_{16}H_{15}O_5NS$ requires C, 57·7; H, 4·5; N, 4·2; S, 9·6%). This *amino-acid* was sparingly soluble in hot water but almost insoluble in benzene. There was no evidence of ring-closure when it was heated alone in nitrobenzene at the b. p. or in concentrated sulphuric acid at 100°.

2-(3-*Diacetylamino*-4-*ethylsulphonylbenzoyl*)*benzoic acid* was obtained when the amino-acid (0·4 g.) was stirred in the cold with acetyl chloride (4 c.c.), acetic acid then added, and the mixture heated to boiling until a clear solution resulted. Addition to water gave a precipitate, which was collected; the *diacetylamino*-compound crystallised from benzene in colourless, irregular-shaped crystals, m. p. 163—164° (Found: C, 57·5; H, 4·5; N, 3·2; S, 7·1. $C_{20}H_{19}O_7NS$ requires C, 57·55; H, 4·6; N, 3·4; S, 7·7%). Only oily products resulted when the amino-acid was heated with acetic anhydride.

Methyl 2-(3-*Amino*-4-*ethylsulphonylbenzoyl*)*benzoate*.—Hydrochloric acid (2N.; 200 c.c.) was added rapidly to a suspension of iron filings (15 g.) in alcohol (250 c.c.) containing methyl 2-(4-ethylsulphonyl-3-nitrobenzoyl)benzoate (10 g.). After 1 hour's refluxing, the suspension was filtered, and the filtrate cooled. The crystalline precipitate was extracted by hot dilute N-hydrochloric acid, and the residue

(7·8 g.) crystallised several times from methyl alcohol. Pale yellow hexagonal plates were obtained, having m. p. 152—153° (Found: C, 58·45; H, 5·2; N, 3·7; S, 9·2. $C_{17}H_{17}O_5NS$ requires C, 58·8; H, 4·9; N, 4·0; S, 9·2%). The same *amino*-ester was obtained in smaller yield and accompanied by oily material when the reduction was carried out by means of zinc and dilute acetic acid. Reduction by iron and hydrochloric acid in acetic acid was also unsuccessful, as also was the use of sodium dithionite in aqueous alcohol or dilute sodium hydroxide. The methyl ester of the amino-acid was hydrolysed to the parent acid by 15 minutes' heating with 5% aqueous sodium hydroxide at the b. p.

Methyl 2-(3-*acetamido*-4-*ethylsulphonylbenzoyl*)*benzoate* was obtained by stirring the amino-ester in the cold with acetyl chloride containing sodium acetate. Recrystallisation from alcohol gave the product as colourless plates, m. p. 143·5—144·5° (Found: N, 3·5; S, 8·1. $C_{19}H_{19}O_6NS$ requires N, 3·6; S, 8·2%). The same product was obtained by heating the amino-ester with acetic anhydride at the b. p. for 3 hours; it was more difficult to purify when made by this method.

1-*Amino*-2-*ethylsulphonylanthraquinone and* 2-*Amino*-3-*ethylsulphonylanthraquinone.*—Methyl 2-(3-amino-4-ethylsulphonylbenzoyl)benzoate (2 g.) was added to concentrated sulphuric acid (50 c.c.), heated quickly to 175°, and kept at 175—180° for 10 minutes. The solution was then cooled and added to water, and the brown precipitate (4·3 g.) collected. The product was extracted first with hot 5% aqueous sodium carbonate, then with benzene. The residue was further extracted with hot nitrobenzene. On cooling, a solid separated and this was crystallised from acetic acid. Yellow needles, m. p. 278—279° (Found: C, 61·45; H, 4·3; N, 4·0; S, 9·9. $C_{16}H_{13}O_4NS$ requires C, 61·0; H, 4·1; N, 4·4; S, 10·2%), of 2-*amino*-3-*ethylsulphonylanthraquinone* were obtained (2·2 g.).

The benzene extract when chromatographed on alumina gave a main orange band and this passed out of the column during development with benzene. The eluate so obtained was evaporated; it furnished 1-*amino*-2-*ethylsulphonylanthraquinone* (0·6 g.) as clusters of small orange crystals, m. p. 217—218° (Found: C, 60·7; H, 4·0; N, 4·6; S, 10·4%). The chromatogram also exhibited a more strongly adsorbed, intensely yellow band from which a small additional quantity of 2-amino-3-ethylsulphonylanthraquinone was obtained.

(i) 1-Amino-2-ethylsulphonylanthraquinone was sparingly soluble in methyl alcohol, but crystallised readily from acetic acid. It dissolved in concentrated sulphuric acid with a reddish-orange colour. The orange solution in pyridine became blue on addition of methyl-alcoholic potassium hydroxide, and greenish-blue, finally yellow-brown, with excess of the reagent. With boric acid in acetic anhydride it gave a deep violet solution. It dissolved in alkaline sodium dithionite, forming a deep red solution. It was recovered unaltered after being heated with acetic anhydride at the b. p. or with toluene-*p*-sulphonyl chloride at 95—100°. Its *acetyl* derivative was prepared by heating it with acetyl chloride in acetic anhydride for 1·5 hours; the brown solution formed was chromatographed on alumina and afforded, in addition to unchanged amine and strongly adsorbed brown material, a yellow band of the *N*-acetyl derivative; elution and recrystallisation from benzene gave yellow needles, m. p. 236·5—237·5° (Found: N, 4·1; S, 9·3. $C_{18}H_{15}O_6NS$ requires N, 3·9; S, 9·0%).

The *benzoyl* derivative, formed when the amine was heated at 100° with benzoyl chloride containing a very small proportion of sulphuric acid, crystallised from alcohol in pale orange silky needles, m. p. 198—199°, softening at 194° (Found: C, 66·5; H, 4·4; N, 3·5; S, 8·4. $C_{23}H_{17}O_5NS$ requires C, 65·9; H, 4·1; N, 3·3; S, 7·6%). The *dibenzoylamino*-derivative resulted on heating of the amine with benzoyl chloride in pyridine at the b. p.; it separated from acetic acid in small clusters of orange crystals, m. p. 280·5—281·5° (Found: C, 68·7; H, 3·9; N, 2·6; S, 6·3. $C_{30}H_{21}O_6NS$ requires C, 68·8; H, 4·0; N, 2·7; S, 6·1%).

(ii) 2-Amino-3-ethylsulphonylanthraquinone was less soluble than its isomer in all the common solvents. It neither reacted with benzoyl chloride containing sulphuric acid at 100° nor formed a deeply coloured derivative with boric acid and acetic anhydride. The orange solution in pyridine became dichroic (green-brown) on addition of methyl-alcoholic potassium hydroxide; the colour was not stable against dilution with methyl alcohol. In alkaline sodium dithionite it dissolved, forming a deep green solution; the colour in concentrated sulphuric acid was orange-red. There was no indication of the formation of a flavanthrone derivative when the amine was heated under reflux for an hour with antimony pentachloride. Its *acetyl* derivative, prepared by heating the amine with acetic anhydride at the b. p. for 5 hours, crystallised from acetic acid in lemon-coloured silky needles, m. p. 224—225° (Found: N, 3·9; S, 8·5. $C_{18}H_{15}O_6NS$ requires N, 3·9; S, 9·0%); and the *benzoyl* derivative, formed by heating the amine with benzoyl chloride in pyridine for 4 hours, crystallised from acetic acid in almost colourless clusters of platelets, m. p. 271·5—272° (Found: N, 3·4; S, 7·6. $C_{23}H_{17}O_5NS$ requires N, 3·3; S, 7·6%).

2-*Amino*-1-*bromo*-3-*ethylsulphonylanthraquinone.*—2-Amino-3-ethylsulphonylanthraquinone (2·5 g.) was heated for 3 hours at 160° with a 1% solution of bromine (49 c.c.; 1·1 mols.) in nitrobenzene. A second portion of the bromine–nitrobenzene solution (20 c.c.) was then added, and the heating resumed at 180° for 2 hours. Finally, a further 20-c.c. portion was added, and the heating continued for 2 hours longer. The product was then cooled, water was added, and the nitrobenzene distilled in steam. The yellow-brown crystalline residue (2·9 g.; m. p. 200—203°) was collected and recrystallised several times from acetic acid. Golden-yellow needles, m. p. 205—207°, were obtained (Found: C, 48·2; H, 3·1; N, 3·8; S, 8·2; Br, 20·15. $C_{16}H_{12}O_4NSBr$ requires C, 48·7; H, 3·0; N, 3·6; S, 8·1; Br, 20·3%). 2-*Amino*-1-*bromo*-3-*ethylsulphonylanthraquinone* dissolved in concentrated sulphuric acid with a red colour, and in alkaline sodium dithionite forming a deep green solution. Methyl-alcoholic potassium hydroxide, added to the yellow solution in pyridine, caused a change in colour to greenish-blue; by reflected light the solution was ruby-red and the colour became more pronounced on warming. The colour showed considerable stability; addition of methyl alcohol caused a change to red-violet, but this persisted even when water was added. A yellow colour resulted on addition of dilute hydrochloric acid. The bromo-amine was unaltered by benzoyl chloride containing a small proportion of sulphuric

acid, at 100° by boiling benzaldehyde during 7 hours, by dry pyridine under reflux for the same time, or by boiling acetic anhydride.

2-Diacetylamino-1-bromo-3-ethylsulphonylanthraquinone.—Obtained by heating the bromo-amine for 6 hours with a solution of acetyl chloride in acetic anhydride, this *diacetylamino*-compound crystallised from acetic acid–methanol in rosettes of yellow plates, m. p. 218—220° (Found: N, 2·95; S, 6·75; Br, 16·55. $C_{20}H_{18}O_6NSBr$ requires N, 2·9; S, 6·7; Br, 16·7%). There was no indication of the formation of a derivative of 1 : 1′-dianthraquinonyl when the diacetyl compound was heated under reflux for 1·5 hours in nitrobenzene containing copper bronze (Scholl and Mansfeld's test, *Ber.*, 1910, **43**, 1734).

3-Ethylsulphonyl-2′-phenyloxazolo(4′ : 5′-2 : 1)anthraquinone.—2-Amino-1-bromo-3-ethylsulphonylanthraquinone (0·4 g.) was heated under reflux during 11 hours with benzoyl chloride (4 c.c.) and pyridine (6 c.c.). The product was added to alcohol and the fine yellow needles (0·1 g., m. p. 306—307°) which separated were crystallised from acetic acid. The pure *oxazolo*-derivative melted at 307—308° after sintering at 295° (Found: C, 66·1; H, 3·2; N, 3·2; S, 7·3. $C_{23}H_{15}O_5NS$ requires C, 66·2; H, 3·6; N, 3·4; S, 7·7%). It dissolved in concentrated sulphuric acid with a yellow colour, and in alkaline aqueous sodium dithionite forming a deep red-violet solution. The yellow solution in pyridine became violet on addition of methyl-alcoholic potassium hydroxide.

3 : 3′-Diethylsulphonylindanthrone.—A solution containing 0·5 g. of 2-amino-1-bromo-3-ethylsulphonylanthraquinone in 5 c.c. of *o*-dichlorobenzene was heated under reflux during 24 hours with cupric acetate (0·01 g.) and anhydrous sodium acetate (0·25 g.). The cooled suspension was filtered, and the residue (0·33 g.) washed first with *o*-dichlorobenzene, then with alcohol, and finally with water. The dried product was powdered and a small portion was shaken on to the surface of concentrated sulphuric acid; the presence of three constituents was indicated by local development of red, brown, and green colours. The main portion was dissolved in cold concentrated sulphuric acid (30 c.c.), and water (15 c.c.) was then added dropwise, the temperature being kept below 50°. On storage, a greenish-blue powder (0·16 g.) separated consisting of *3 : 3′-diethylsulphonylindanthrone* (Found: C, 60·4; H, 3·5; N, 4·3; S, 9·8. $C_{32}H_{22}O_6N_2S_2$ requires C, 61·35; H, 3·5; N, 4·5; S, 10·2%). The sulphuric acid mother-liquor was red and contained mainly unchanged 2-amino-1-bromo-3-ethylsulphonylanthraquinone.

3 : 3′-Diethylsulphonylindanthrone was also the main product when 2-amino-1-bromo-3-ethylsulphonylanthraquinone (0·5 g.) was heated with copper bronze (0·5 g.) in nitrobenzene (5 c.c.). There was no indication of the formation of 3 : 3′-diethylsulphonylflavanthrone. 3 : 3′-Diethylsulphonylindanthrone dissolved in cold α-chloronaphthalene. A 0·002% solution was almost saturated. This exhibited maximum light absorption at 7050 Å ($\varepsilon = 2{\cdot}60 \times 10^4$) and at 6525 Å ($\varepsilon = 1{\cdot}91 \times 10^4$). In concentrated sulphuric acid a 0·002% solution was green. There was strong absorption in the red, but no maximum absorption in the visible region. In contrast, similar solutions of indanthrone and its 3 : 3′-dichloro- and 3 : 3′-dibromo-derivatives exhibited maximum absorption at 4700 Å. The following observations were made:

	$\varepsilon \times 10^{-4}$: at 4700 Å	at 7000 Å
Indanthrone	1·25	0·82
3 : 3′-Dichloroindanthrone	1·37	0·92
3 : 3′-Dibromoindanthrone	1·32	0·82
3 : 3′-Diethylsulphonylindanthrone	0·59	2·24
3 : 3′-Dibutylsulphonylindanthrone *	0·49	2·25

* For preparation, see p. 2184.

When heated, 3 : 3′-diethylsulphonylindanthrone sinters at about 400° and chars at 500°. It dissolves in concentrated nitric acid, forming a yellow-brown solution, changed to orange-red on warming. In cold pyridine it forms a pale greenish-blue solution. Addition of methyl alcohol changes the colour to dull olive-green, and the further addition of methyl alcohol to green; ultimately the solution becomes yellower and a brown precipitate separates. Heated with quinoline, 3 : 3′-diethylsulphonylindanthrone dissolves and blue needles having a reddish metallic lustre separate. The product does not contain sulphur; it dissolves in concentrated sulphuric acid forming a brown solution the absorption spectrum of which is identical with that of indanthrone (Found: C, 74·5; H, 3·4; N, 6·3. Calc. for $C_{28}H_{14}O_4N_2$: C, 76·0; H, 3·2; N, 6·3%). Heating with dry piperidine gives the same product (Found: N, 6·3%). 3 : 3′-Diethylsulphonylindanthrone proved to be more stable towards the oxidising action of hypochlorites than indanthrone or either of its halogen derivatives when tested by the standard procedure (*J. Soc. Dyers Col.*, 1948, **64**, 133). 8N-Nitric acid being used as oxidant (cf. H. B. Bradley and Derrett-Smith, *ibid.*, 1940, **56**, 97), 3 : 3′-diethylsulphonylindanthrone was rendered greenish-yellow more readily even than indanthrone.

A suspension was prepared by dispersing 3 : 3′-diethylsulphonylindanthrone (0·03 g.) at 50° in 5% aqueous sodium hydroxide (3 c.c.) containing sodium dithionite (0·1 g.). After 10 minutes, water (30 c.c.) was added at 50° and the green suspension was kept at the same temperature for 40 minutes. The suspension was then aerated, and the precipitate collected and washed. It resembled the original material in properties. Analysis indicated the loss of approx. 20% of the ethylsulphonyl substituents present initially (Found: S, 8·2%). In a similar experiment, 0·03 g. of 3 : 3′-dichloroindanthrone being used, and the resulting solution filtered, it was found that 45% of the chlorine substituents present initially was lost after 90 minutes at 50° (Found: Cl, 7·7. Calc. for $C_{28}H_{12}O_4N_2Cl_2$: Cl, 13·9%).

2-(4-Butylthio-3-nitrobenzoyl)benzoic Acid.—Prepared by the method described for the ethyl analogue, butanethiol (3·55 c.c.) being employed instead of ethanethiol (2·65 c.c.), a crude product, m. p. about 140°, was obtained in a yield of 11·5 g. Purification was effected by chromatography on alumina and

repeated crystallisation from acetic acid. Pale yellow, silky needles of the *acid* were obtained, m. p. 154—155° (Found: N, 4·0; S, 9·2. $C_{18}H_{17}O_5NS$ requires N, 3·9; S, 8·9%).

2-(4-*Butylsulphonyl*-3-*nitrobenzoyl*)*benzoic Acid.*—The butylthio-acid (13 g.), dissolved in acetic acid (100 c.c.), was heated on the steam-bath for 6 hours with hydrogen peroxide (18 c.c.; 90-vol.). Evaporation to small bulk gave the *butylsulphonyl acid* (8·5 g.; m. p. 140—148°). Repeated crystallisation from acetic acid afforded colourless needles, m. p. 147—149° (Found: N, 3·8; S, 7·9. $C_{18}H_{17}O_7NS$ requires N, 3·6; S, 8·2%).

2-(3-*Amino*-4-*butylsulphonylbenzoyl*)*benzoic Acid.*—Iron filings (10 g.), water (100 c.c.), and concentrated hydrochloric acid (10 c.c.) were added to a solution containing the *m*-nitro-acid (6·5 g.) in acetic acid (100 c.c.). After 1 hour's refluxing, the suspension was filtered, the filtrate mixed with a small volume of water, and the crystalline precipitate collected. The product was extracted by 3·5% hydrochloric acid, and the residual, almost colourless plates (5·1 g.; m. p. 168—170°) recrystallised from aqueous acetic acid. The pure *amino-acid* had m. p. 170—172° (Found: N, 4·1; S, 9·0. $C_{18}H_{19}O_5NS$ requires N, 3·9; S, 8·9%).

1-*Amino*-2-*butylsulphonylanthraquinone and* 2-*Amino*-3-*butylsulphonylanthraquinone.*—A solution of the amino-acid (3 g.) in concentrated sulphuric acid (30 c.c.) was heated for an hour at 130°, then cooled and added to water. The precipitate was extracted with 5% aqueous sodium carbonate, and the residue (2·5 g.) crystallised three times from acetic acid. 2-*Amino*-3-*butylsulphonylanthraquinone* was thus obtained in fine, yellow needles (0·7 g.), m. p. 250—251° (Found: C, 62·6; H, 4·5; N, 4·1; S, 9·2. $C_{18}H_{17}O_4NS$ requires C, 63·0; H, 5·0; N, 4·1; S, 9·3%). The mother-liquors were evaporated to dryness, and the residue chromatographed in benzene on alumina. By this means was obtained 0·25 g. of 1-*amino*-2-*butylsulphonylanthraquinone*, which crystallised from absolute alcohol in silky, orange-red needles, m. p. 187—188° (Found: C, 63·6; H, 4·6; N, 3·9; S, 8·9%).

1-Amino-2-butylsulphonylanthraquinone dissolved in pyridine, forming an orange-yellow solution; this was changed to greenish-blue by addition of methyl-alcoholic potassium hydroxide and to orange-yellow by further addition of methyl alcohol. It dissolved in aqueous alkaline sodium dithionite with an orange-red colour.

2-Amino-3-butylsulphonylanthraquinone formed a yellow solution in pyridine, changed to red-violet (green by reflected light) by methyl-alcoholic potassium hydroxide. The initial colour was restored by methyl alcohol. It dissolved in aqueous alkaline sodium dithionite, forming a green solution.

2-*Amino*-1-*bromo*-3-*butylsulphonylanthraquinone.*—To a solution containing 2-amino-3-butylsulphonylanthraquinone (2 g.) in nitrobenzene (20 c.c.) were added 35 c.c. (1·1 mols.) of a 1% solution of bromine in the same solvent. After 3 hours' heating at 160° a further 16 c.c. of the bromine–nitrobenzene solution was added, and the heating continued at 170—180° for 3 hours. The solvent was then distilled in steam and the greenish-yellow residue (2·4 g.) was chromatographed in benzene on alumina. Of several bands the most mobile was a broad yellow zone. This passed through the column during development with benzene. The eluate was evaporated, and the residue crystallised twice from absolute alcohol. The *bromo*-compound consisted of golden-yellow plates and rods (1·0 g.), m. p. 184—185° (Found: C, 50·0, 50·0; H, 4·0, 3·9; N, 3·3; S, 7·2; Br, 18·2. $C_{18}H_{16}O_4NSBr$ requires C, 51·2; H, 3·8; N, 3·3; S, 7·6; Br, 18·95%). A small amount of unchanged 2-amino-3-butylsulphonylanthraquinone was present on the chromatogram, as well as a strongly adsorbed brown substance. A solution of the bromo-derivative in pyridine was yellow, changed to red-violet (blue in thin layers) when methyl-alcoholic potassium hydroxide was added. The restoration of a yellow colour occurred only after the addition of a relatively large volume of methyl alcohol. The bromo-derivative forms a green solution in alkaline sodium dithionite.

3 : 3′-*Dibutylsulphonylindanthrone.*—The self-condensation of 2-amino-1-bromo-3-butylsulphonylanthraquinone was carried out under the same conditions as used in the analogous reaction with the 3-ethylsulphonyl compound (p. 2183). The crude *indanthrone* (0·16 g.) crystallised from *o*-dichlorobenzene in blue needles (0·13 g.) having a reddish lustre (Found: C, 62·55; H, 4·2; N, 4·0; S, 9·2. $C_{36}H_{36}O_8N_2S_2$ requires C, 63·3; H, 4·4; N, 4·1; S, 9·4%). On heating, the product decomposed at 377° (uncorr.). It was more soluble in the common organic solvents than the ethyl analogue. The solution in α-chloronaphthalene showed light absorption maxima at 7050 A. and 6550 A. The greenish-blue solution in hot pyridine became greenish-yellow on addition of methyl-alcoholic potassium hydroxide. It formed a green solution in concentrated sulphuric acid, changed to yellowish-brown by nitric acid. When finely dispersed, it was very sparingly soluble in aqueous alkaline sodium dithionite, and, when it was treated by the procedure described for the ethyl homologue, the butylsulphonyl substituent was at least as stable as the ethylsulphonyl (Found, in material recovered from a suspension of the reduced form after being kept at 50° for 40 minutes: S, 8·1%).

The following *iso*propyl compounds were prepared from 2-(4-chloro-3-nitrobenzoyl)benzoic acid by the procedure employed for the ethyl homologue. 2-(3-*Nitro*-4-iso*propylthiobenzoyl*)*benzoic acid* crystallised from acetic acid in yellow nodules (77% yield), m. p. 177—180° (Found: N, 4·0; S, 9·2. $C_{17}H_{15}O_5NS$ requires N, 4·1; S, 9·3%). The *methyl* ester crystallised from methyl alcohol in yellow cubes, m. p. 83—85° (Found: N, 4·3; S, 9·3. $C_{18}H_{17}O_5NS$ requires N, 3·9; S, 8·9%). 2-(3-*Nitro*-4-iso*propylsulphonylbenzoyl*)*benzoic acid* separated from solution in acetic acid as a colourless, crystalline mass (yield, 70%), m. p. 186—188° (Found: C, 54·3; H, 4·0; N, 3·7; S, 8·5. $C_{17}H_{15}O_7NS$ requires C, 54·1; H, 4·0; N, 3·7; S, 8·5%). 2-(3-*Amino*-4-iso*propylsulphonylbenzoyl*)*benzoic acid*, prepared in poor yield by reducing the 3′-nitro-acid, crystallised from benzene in colourless plates, m. p. 179—182° (Found: C, 58·3; H, 4·9; N, 3·8; S, 8·9. $C_{17}H_{17}O_5NS$ requires C, 58·8; H, 4·9; N, 4·0; S, 9·2%). The *methyl* ester separated from methyl alcohol in colourless, stout prisms, m. p. 166·5—167° (Found: N, 4·2; S, 9·1. $C_{18}H_{19}O_5NS$ requires N, 3·9; S, 8·9%). 2-*Amino*-3-iso*propylsulphonylanthraquinone* resulted in poor yield by cyclising the corresponding amino-acid. It crystallised from

absolute alcohol in yellow needles, m. p. 252—253° (Found: N, 4·6; S, 9·7. $C_{17}H_{16}O_4NS$ requires N, 4·3; S, 9·7%).

1-p-*Chlorophenyl*-4-*hydroxyphthalazine*.—Colourless platelets (0·97 g.) separated when 2-*p*-chlorobenzoylbenzoic acid (1 g.) was heated under reflux for 1·5 hours with 100% hydrazine hydrate (3 c.c.). Crystallisation from toluene did not raise the m. p., 268—270° (Found: N, 11·2; Cl, 13·8. $C_{14}H_9ON_2Cl$ requires N, 10·9; Cl, 13·8%). The *phthalazine* was insoluble in concentrated hydrochloric acid or hot 5% aqueous sodium carbonate, but it dissolved in hot 5% aqueous sodium hydroxide. It dissolved in hot alcohol, acetone, or acetic acid, but not in ligroin.

The authors thank the University of Leeds for the award of a Bradford Dyers' Association Research Fellowship to one of them (H. E. N.).

CLOTHWORKERS RESEARCH LABORATORY,
THE UNIVERSITY, LEEDS.

[*Received, April 27th*, 1951.]

---

476. *Dimethin*merocyanines *derived from* 2-*Substituted Azol*-5-*ones*.*

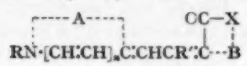
By PER AUBERT, E. B. KNOTT, and L. A. WILLIAMS.

A number of *S*-esters (V), including long-chain alkyl esters, of *N*-dithiocarboxyglycine have been prepared, cyclised by the method of Cook, Harris, Heilbron, and Shaw (*J.*, 1948, 1056), and converted into a series of dimethin*mero*cyanines (cf. Cook, Harris, and Shaw, *J.*, 1949, 1435) containing the 2-alkylthiothiazol-5-one nucleus. Analogous *O*-esters (XIV) of *N*-thioncarboxyglycine were readily obtained by the condensation of potassium aminoacetate with ethyl alkoxydithioformates. Cyclisation of these with acetic anhydride gave a series of 2-alkoxythiazol-5-ones (XV), or, in the presence of ethyl orthoformate, 2-alkoxy-4-ethoxymethylenethiazol-5-ones (XVI) both of which were converted into a series of dimethin*mero*cyanines. Similarly *N*-acylthiohydantoic acids were cyclised by phosphorus tribromide to give what are believed to be 2-acylamidothiazol-5-one hydrobromides which also contain a reactive methylene group giving rise to a series of dimethin*mero*cyanines.

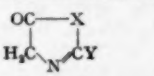
The condensation of *N*-dithiocarbethoxyglycine with secondary amines led to *NN*-disubstituted *N'*-carboxythioureas (XIX) which were cyclised by phosphorus tribromide to 2-di-alkyl(or -aryl)aminothiazol-5-ones which also readily formed dimethin*mero*cyanines.

The series of dimethin*mero*cyanines derived from 2-phenyloxazol-5-one (Cook *et al.*, *loc. cit.*, 1949) was extended.

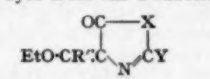
BECAUSE of their usefulness as photographic optical sensitisers the class of dyes known as dimethin*mero*cyanines (I) has been widely investigated. In (I), R is usually alkyl, R' is hydrogen, alkyl, or aryl, *n* is 0 or 1, and A and B represent the atoms necessary to complete a 5- or 6-membered ring or rings. In the majority of known dyes the ketonic nucleus carries a substituted amino-group adjacent to the ketonic group (*i.e.*, X = NR). Keyes and Brooker (B.P. 518,904), however, obtained a number of dimethin*mero*cyanines containing the 2-phenyloxazol-5-one nucleus (II; X = O, Y = Ph), and recently Cook *et al.* (*J.*, 1949, 1435) obtained similar dyes by a different method and also related dyes from the 2-substituted thiazol-5-one



(I.)



(II.)



(III.)

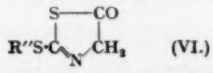
(IV.)

nucleus (II; X = S, Y = Ph, ·S·CH_2Ph, ·S·CO_2Et) The latter authors prepared their dyes by the known procedure of condensing the 4-ethoxymethylene derivative (III; R' = H) of (II) with the reactive methyl derivative of the required cyclic quaternary ammonium salt in the presence of alcoholic triethylamine.

In view of the possible photographic application of such dyes a larger number have been synthesised (see Experimental) containing the 2-phenyloxazol-5-one, 2-ethylthiothiazol-5-one, 2-benzylthiothiazol-5-one, and 2-mercaptothiazol-5-one nuclei (cf. II; X = S, Y = SH) (Cook, Heilbron, and Levy, *J.*, 1948, 201). These dyes were obtained both by Cook's method

* Patent applications pending.

and by the more usual method of condensing (II) with the 2-acetanilidovinyl derivative of the cyclic quaternary ammonium salt in alcoholic triethylamine. An extension of the series of dyes was made possible (see Experimental) by the synthesis of a number of further *S*-esters (V) of *N*-dithiocarboxyglycine. Thus, using Körner's method (*Ber.*, 1908, **41**, 1091), the *p*- and *m*-nitrobenzyl esters (V; R'' = $\cdot CH_2 \cdot C_6H_4 \cdot NO_2$) were obtained and cyclised by phosphorus tribromide to the required hydrobromides of 2-*p*- and 2-*m*-nitrobenzylthiothiazol-5-one (VI). It was also possible to make long-chain alkyl esters (V), by refluxing the required alkyl bromide with the potassium salt of *N*-dithiocarboxyglycine. In this way the *n*-hexyl, *n*-heptyl, *n*-octyl, *n*-decyl, *n*-dodecyl, and 3-phenylpropyl esters (V) were readily obtained. The salts of the longer-chain esters possess some surface activity. All of these esters were readily cyclised by

(V.) $R''S_2C \cdot NH \cdot CH_2 \cdot CO_2H \longrightarrow$  (VI.)

acetic anhydride or phosphorus tribromide to the required thiazol-5-one (VI) or its hydrobromide (VI; R'' = $C_{12}H_{25}$) was characterised by conversion of its hydrobromide into 2-*n*-dodecylthio-5-hydroxy-4-phenylazothiazole (IV; R = $S \cdot C_{12}H_{25}$) by gently warming it with diazoaminobenzene in ethanol (see also Knott and Williams, *J.*, 1951, 1586, for similar reactions of diazoaminobenzene with reactive methyl groups).

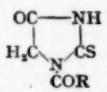
All of the above thiazol-5-ones or their 4-ethoxymethylene derivatives were readily converted into dimethin*mero*cyanine dyes. It has also been found that chain-substituted dyes (I; R' = Me or Et) are readily obtained from the intermediates (III; R' = Me or Et) prepared by cyclisation of the necessary glycine with acetic anhydride in the presence of ethyl orthoacetate or ethyl orthopropionate. Although these intermediates were not isolated in the thiazol-5-one series, crystalline 4-1'-ethoxyethylidene-2-phenyloxazol-5-one (III; R' = Me, X = O, Y = Ph) * (cf. "The Chemistry of Penicillin," Princeton Univ. Press, 1949, p. 803, for III, R' = H) was isolated in good yield.

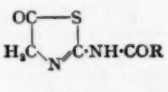
In view of the strong sensitising properties of many of the foregoing dyes we prepared analogues with other substituents in the 2-position of the thiazol-5-one ring, notably 2-acylamido-, 2-alkoxy-, and 2-*tert.*-amino-groups. The requisite thiazolones were hitherto unknown.

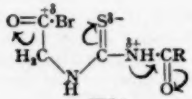
2-*Acylamidothiazol-5-ones* (X).—Wheeler, Nicolet, and Johnson (*Amer. Chem. J.*, 1911, **46**, 456) obtained *N*-acetylthiohydantoic acid (*N*-*N'*-acetylthiocarbamylglycine) (VIII; R = Me) by heating potassium aminoacetate with ethyl acetamidodithioformate (VII; R = Me). They obtained the benzamido-analogue (VIII; R = Ph) by a similar process. On heating these

$R \cdot CO \cdot NH \cdot CS_2Et \xrightarrow{NH_2 \cdot CH_2 \cdot CO_2K} R \cdot CO \cdot NH \cdot CS \cdot NH \cdot CH_2 \cdot CO_2H$

(VII.) (VIII.)

 (IX.)

 (X.)

 (XI.)

acids with a mixture of acetic anhydride, acetic acid, sodium acetate, and benzaldehyde they obtained a compound which they formulated as 1-acetyl-5-benzylidenetetrahydro-4-keto-2-thioglyoxaline (the benzylidene derivative of IX; R = Me) since on hydrolysis with cold 10% potassium hydroxide it yielded 5-benzylidenetetrahydro-4-keto-2-thioglyoxaline which was synthesised unambiguously from 2-thiohydantoin and benzaldehyde.

It will be observed that (VIII) is an acylamide of *N*-dithiocarboxyglycine, the *S*-ester of which was used by Cook in the synthesis of 2-alkylthiothiazol-5-ones, and that (VIII) is thus the intermediate required for cyclisation to 2-acylamidothiazol-5-ones. The above work (Wheeler *et al.*) indicates, however, that ring closure occurs between the carboxy-group and the amido-nitrogen atom and not between the former and the sulphur atom. Treatment of (VIII; R = Me) with acetic anhydride under conditions used by Cook for the cyclisation of *N*-dithiocarbalkoxyglycines gave an oil which exhibited only weak colour reactions with an alcoholic-triethylamine solution of a variety of 2-acetanilidovinyl derivatives of cyclic quaternary

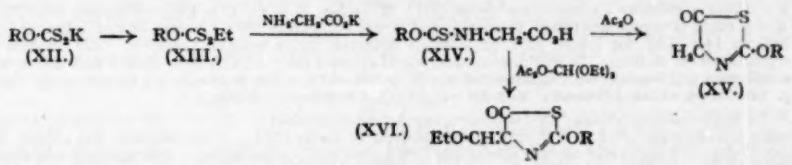
* This compound has already been made by Kendall and Duffin (B.P. 633,736).

ammonium salts. On the other hand treatment of (VIII; R = Me) with phosphorus tribromide in dioxan–ether gave a product, the analysis of which indicated the loss of the elements of water, giving the hydrobromide of (IX) or (X). Similar products were obtained from (VIII; R = Bu^n or Ph). All these hydrobromides slowly decomposed in moist air, fuming strongly. They gave strong colour reactions with the above-mentioned quaternary salts, and a number of dimethin*mero*cyanines were isolated (see Experimental). Attempts to isolate the free bases from the hydrobromides by shaking them with aqueous sodium acetate–ether were unsuccessful, the ethereal layer no longer giving any colour reactions. This method of releasing the bases was successfully employed by Cook *et al.* (*loc. cit.*, 1949) in the case of 2-benzylthiothiazol-5-one.

The apparent instability of the bases of these hydrobromides is considered to favour their being thiazolones (X) rather than tetrahydroketoglyoxalines (IX) since the latter would be expected to be stable. Further evidence against (IX) is the non-formation of insoluble silver salts by the dyes derived from the hydrobromides. Thus the thiol group in (IX) (regarded as a mercapto-derivative) should be capable of salt formation as has been found for similar dyes derived from 2-mercaptothiazol-5-one. From an electronic standpoint it would, moreover, be expected that thiazolone formation would be preferred. Thus it may be assumed that the first step in the cyclisation is the formation of the acid bromide (XI) in which one reactive centre is the electrophilic carbonyl-carbon atom of the COBr residue. For formation of (IX) it is then required that this centre should attack the amido-nitrogen atom which is, however, also electrophilic by virtue of the amide-type resonance in the system. For thiazolone formation the nucleophilic sulphur atom is the second active centre and consequently the formation of a covalent C–S bond appears the more likely. Similar electronic conditions also apply in the condensation of thiourea with α-halogeno-ketones or 2-bromoethylamine, the resultant products in such cases being derivatives of 2-aminothiazole or 2-aminothiazoline and not of a di- or tetra-hydroglyoxaline. In view of the sensitivity of 5-imino-2-thiothiazolidines to alkali (Cook *et al.*, *J.*, 1948, 201) (causing isomerisation to 2 : 4-dithiohydantoin) there appears the possibility that the compound obtained by Wheeler *et al.* (*loc. cit.*) was, in fact, a thiazolidone, the hydrolysing treatment with alkali causing a similar isomerisation to the 2-thiohydantoin derivatives.

The hydrobromide from (VIII; R = Pr^n) condensed readily with diazoaminobenzene to give what is considered to be 2-*n*-butyramido-5-hydroxy-4-phenylazothiazole (IV; R = NH·$COPr^n$).

2-*Alkoxythiazol-5-ones* (XV).—For the preparation of these derivatives, *N*-thiocarbalkoxyglycines (XIV) were required. They cannot be obtained in the same way as the *N*-dithio-analogues, but are readily obtained according to the following reaction scheme:

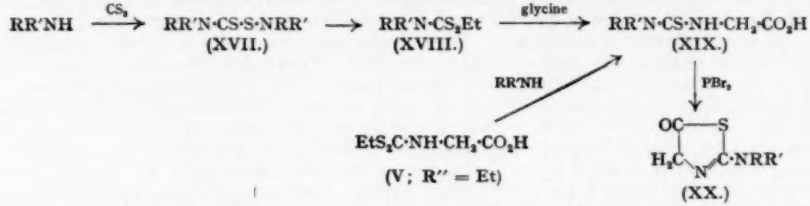


The required alcohol (ROH) was converted into the potassium alkoxydithioformate (alkylxanthate) (XII), esterified with ethyl bromide to give the ethyl alkoxydithioformate (XIII) (omission of this step lowers considerably the yield in the next step), and the latter refluxed with aqueous-alcoholic potassium aminoacetate to give the required *N*-thioncarbalkoxyglycine (XIV) with the elimination of ethanethiol. Twelve alkyl, and also the 3-phenylpropyl, esters were thus prepared; they are all stable, alkali-soluble crystalline solids, the longer-chain esters being surface-active. They are readily cyclised by acetic anhydride at 100—130° to a series of 2-alkoxythiazol-5-ones. The crude oils were used in all cases for the preparation of a series of dimethin*mero*cyanines. 2-Ethoxythiazol-5-one was distilled without decomposition but the product, even after fractionation, had the odour of acetic anhydride and gave low values for nitrogen and sulphur.

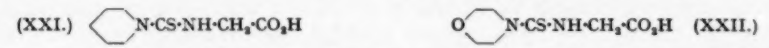
By cyclising in the presence of ethyl orthoformate 2-alkoxy-4-ethoxymethylenethiazol-5-ones (XVI) were obtained and the crude products used in dye formation. They are all crystalline products but those with short alkyl chains rapidly decompose and liquefy. The stability increases with increasing chain length and several of these compounds were characterised.

The attempted cyclisation of (XIV) by phosphorus tribromide or phosphorus trichloride in dioxan–benzene did not give the required 2-alkoxythiazol-5-one salt. The crystalline product which resulted was well defined and its nature and properties will be reported separately.

2-tert.-*Aminothiazol-5-ones* (XX).—In view of the failure to bring 2-ethylthiothiazol-5-one into reaction with secondary amines in order to produce 2-*tert.*-aminothiazol-5-ones their synthesis was attempted by the cyclodehydration of *NN*-disubstituted *N'*-carboxymethylthioureas (XIX). In theory these may be obtained by two routes. It is well known (Delépine, *Compt. rend.*, **1902**, **134**, 715) that secondary amines (NHRR') condense with carbon disulphide to give salts of *NN*-disubstituted dithiocarbamates (XVII) which are readily esterified by alkyl halides to give (XVIII). Treatment of these esters with glycine would then be expected to give the amide (XIX) but it appears that amide formation does not readily occur in these cases, although it occurs much more readily with *N*-monosubstituted dithiocarbamates (XVIII; R = H).



It was found then that the required substances were smoothly formed by the condensation of the secondary amine in aqueous or aqueous-alcoholic solution with the potassium salt of *N*-dithiocarbethoxyglycine (V; R'' = Et). In this way *N*-(*NN*-diethylthiocarbamyl)glycine (XIX;



R = R' = Et), and the analogues (XIX; R = Ph, R' = Et), (XXI), and (XXII) were obtained. These are cyclised by phosphorus tribromide to oily 2-*tert.*-aminothiazol-5-one hydrobromides which were used directly in dye formation (see Experimental).

Experimental.

Microanalyses are by Drs. Weiler and Strauss, Oxford. M. p.s are uncorrected.

4-1'-*Ethoxyethylidene-2-phenyloxazol-5-one* (III; R' = Me, X = O, Y = Ph).—Hippuric acid (72 g., 0·4 mol.), ethyl orthoacetate (65 g., 0·4 mol.), and acetic anhydride (80 c.c.) were heated together in an oil-bath at 140—150° for 1 hour and the solvents removed under reduced pressure. The residual red oil crystallised on chilling. It was dissolved in warm ethanol (50 c.c.) and then chilled and the crystals were collected and washed with light petroleum (b. p. 60—80°). The *ketone* (21 g.) formed pink blades, m. p. 110°, from ethanol (Found: N, 5·95. $C_{13}H_{13}O_3N$ requires N, 6·05%).

N-Dithiocarbalkoxyglycines.—*N-Dithiocarbonitrobenzyloxyglycines* (V; R'' = $CH_2{\cdot}C_6H_4{\cdot}NO_2$). Potassium hydroxide (11·2 g., 0·2 mol.) was dissolved in water (25 c.c.), the solution was chilled, and glycine (7·5 g., 0·1 mol.) and carbon disulphide (7·6 g., 0·1 mol.) were added. The mixture was shaken until homogeneous (3—4 hours) and *m*-nitrobenzyl bromide (21·6 g., 0·1 mol.) dissolved in ethanol (25 c.c.) was added. After further shaking for 4 hours the yellow solid (not investigated) was filtered off and the filtrate acidified to give an oil which soon crystallised. It was redissolved in 2N-sodium carbonate, and the solution filtered and acidified. The precipitated m-*nitrobenzyl* ester was collected, washed and air-dried. It (14 g.) formed pale yellow needles, m. p. 144°, from benzene (Found: S, 22·5. $C_{10}H_{10}O_4N_2S_2$ requires S, 22·4%). The p-*nitro*-isomer was similarly obtained from *p*-nitrobenzyl chloride (17·15 g., 0·1 mol.). The crude product was crystallised by dissolving it in acetone, adding benzene (2 vols.), and slowly distilling off the acetone. It (20·5 g., 72%) formed pale yellow needles, m. p. 146°, from toluene (Found: S, 22·75%).

N-Dithiocarbo-n-heptyloxyglycine (V; R'' = n-C_7H_{15}). A solution of potassium hydroxide (56 g., 1·0 mol.) and glycine (37·5 g., 0·5 mol.) in water (100 c.c.) was shaken for 3 hours with carbon disulphide (38 g.). *n*-Heptyl bromide (90 g., 0·5 mol.) and industrial alcohol (100 c.c.) were added and the two-phase mixture was refluxed on the steam-bath for 30 minutes. Before the whole finally became homogeneous a third liquid phase separated. The solution was chilled, water (200 c.c.) was added, the resultant cloudiness removed by ether-extraction, and the aqueous layer acidified. The precipitated oil was extracted with ether, the ethereal solution dried, and the solvent distilled off. The residual oil was dissolved in light petroleum (b. p. 80—100°) (300 c.c.) and the solution chilled. There were obtained 57 g. (46%) of glittering, waxy flakes, m. p. 99°, after a second recrystallisation from light petroleum (Found: S, 25·65. $C_{10}H_{19}O_2NS_2$ requires S, 25·7%).

By proceeding similarly the esters recorded in Table I were obtained.

2-p-*Nitrobenzylthiothiazol-5-one Hydrobromide.*—This was obtained in quantitative yield by dissolving (V; R'' = $\cdot CH_2 \cdot C_6H_4 \cdot NO_2$) (20 g.) in dioxan (80 c.c.) and adding ether (100 c.c.) and then phosphorus tribromide (12 c.c.). The required *salt* separated as an oil which rapidly crystallised. It was finely ground under ether and air-dried (Found: Br, 22·3. $C_{10}H_8O_3N_2S_2$,HBr requires Br, 22·9%). The m-*nitro*-isomer was similarly obtained (Found: Br, 22·4%). They both had indefinite m. p.s.

2-Alkylthio-4-1′-ethoxyethylidenethiazol-5-ones and 2-alkylthio-4-1′-ethoxypropylidenethiazol-5-ones were obtained by heating the *N*-dithiocarbalkoxyglycine (15—20 g.), acetic anhydride (75 c.c.), and ethyl orthoacetate or ethyl orthopropionate (30 c.c.) for 30 minutes in an oil-bath at 130°. Removal of the solvents under reduced pressure gave crude oils which were used directly in dye condensations.

2-n-*Dodecylthio-5-hydroxy-4-phenylazothiazole* (IV; R = $\cdot S \cdot C_{12}H_{25}$).—To a solution of *N*-dithiocarbo-n-dodecyloxyglycine (3·2 g.) in dioxan (10 c.c.) and ether (30 c.c.) was added phosphorus tribromide (2 c.c.), and the whole was refluxed for 3 minutes. The solution was chilled and the required 2-n-dodecylthiothiazol-5-one hydrobromide precipitated as an oil by the addition of light petroleum (b. p. 40—60°; 100 c.c.). The oil was washed with ether by decantation and dissolved in ethanol (20 c.c.), and diazoaminobenzene (2 g.) was added. The solution was heated on the steam-bath (*ca.* 1 minute) until effervescence commenced, the flask removed from the bath, and, after being chilled overnight, the *dye* was collected. It (1·4 g.) formed glossy golden plates, m. p. 83°, from light petroleum (b. p. 60—80°) (Found: N, 10·15. $C_{21}H_{31}ON_3S_2$ requires N, 10·4%).

TABLE I.

R'' in (V).	Appearance.	M. p.	Solvent.*	Formula.	Found, S, %.	Reqd., S, %.
n-*Hexyl*	Soft, glistening plates	95°	Ligroin	$C_9H_{17}O_2NS_2$	27·3	27·2
n-*Octyl*	Glossy, waxy plates	100	Light petroleum	$C_{11}H_{21}O_2NS_2$	23·95	24·35
n-*Decyl*	Glittering plates	100	Benzene–light petroleum	$C_{13}H_{25}O_2NS_2$	22·5	22·1
n-*Dodecyl*	Glossy plates	111	Ligroin	$C_{15}H_{29}O_2NS_2$	20·3	20·05
3-*Phenylpropyl*	Waxy plates	122	Benzene–light petroleum	$C_{12}H_{15}O_2NS_2$	24·5	24·8

* Ligroin had b. p. 100—120°. Light petroleum had b. p. 60—80°.

Ethyl n-*Butyramidodithioformate* (VII; R = Pr^n).—Ethyl dithiocarbamate (ethyl aminodithioformate) (Delépine, *Compt. rend.*, 1902, **135**, 975) (25 g.) and butyric anhydride (36 c.c.) were heated at 120° in an oil-bath for 4 hours and the solvents removed under reduced pressure. The residue crystallised on chilling. It was dissolved in methanol at 25° and water run in until slightly turbid. After being seeded and cooled to 5° the *ester* (29·5 g., 75%) separated as long, yellow needles. A sample formed lemon-yellow needles, m. p. 45°, from aqueous methanol (Found: S, 16·55. $C_7H_{13}ONS_2$ requires S, 16·75%).

N-N′-*Butyrylthiocarbamylglycine* (VIII; R = Pr^n).—The above ester (25 g.) was added to a solution of potassium hydroxide (7·5 g.) and glycine (10 g.) in water (30 c.c.) and alcohol (30 c.c.), and the whole refluxed on the steam-bath for 8 hours. The clear solution was concentrated to half volume, water (50 c.c.) added, and the mixture acidified with concentrated hydrochloric acid. The bulky white precipitate was collected, washed with water, and obtained as cream-coloured needles (16 g., 60%), m. p. 180°, from aqueous ethanol (Found: S, 15·95. $C_7H_{12}O_3N_2S$ requires S, 15·7%).

2-*Acylamidothiazol-5-one Hydrobromides.*—The *NN′*-acylthiocarbamylglycine (10 g.) was dissolved in dioxan (50—75 c.c.) and ether (100—150 c.c.), and phosphorus tribromide (518 c.c.) added. The required hydrobromide separated rapidly in *ca.* 95% yield. After 3 hours the solid was collected, washed with ether, and vacuum-dried. They all formed colourless powders which fumed in moist air and gradually decomposed. 2-*Acetamidothiazol-5-one hydrobromide* has m. p. 195° (decomp.) (Found: N, 11·9; Br, 32·9; S, 13·7. $C_5H_6O_2N_2S$,HBr requires N, 11·7; Br, 33·45; S, 13·4%). 2-*Butyramidothiazol-5-one hydrobromide* has m. p. 220° (decomp.) (Found: Br, 29·5. $C_7H_{10}O_2N_2$,HBr requires Br, 30·0%). 2-*Benzamidothiazol-5-one hydrobromide* has m. p. 190° (decomp.) (Found: Br, 24·7. $C_{10}H_8O_2N_2S$,HBr requires Br, 26·6%).

2-*Butyramido-5-hydroxy-4-phenylazothiazole* (IV; R = $NHPr^n$).—2-Butyramidothiazol-5-one hydrobromide (1 g.), diazoaminobenzene (1·35 g.), and ethanol (10 c.c.) were warmed together on the steam-bath until effervescence occurred (1—2 minutes). When the mixture was then set aside the *dye* crystallised and formed golden-orange crystals (0·3 g.), m. p. 251°, from ethanol (Found: N, 19·4. $C_{13}H_{14}O_2N_4S$ requires N, 19·8%).

N-*Thiocarbalkoxyglycines* (XIV).—The potassium alkoxydithioformates (xanthates) were obtained by the method of de la Provostaye and Desains (*Compt. rend.*, 1942, **215**, 593) by dissolving the required alcohol (1 mol.) in carbon disulphide (100—250 c.c.), adding finely powdered potassium hydroxide (1 mol.), and shaking the mixture for 1—2 hours. After chilling, the crude filtered salts were washed with ether and air-dried. They were converted into the esters (ethyl alkoxydithioformates) by addition of ethyl bromide (1 mol.) to a suspension of them (1 mol.) in ethanol and warming if necessary to start the reaction. The thick meal of potassium bromide was dissolved in water, the oily ester extracted with ether and dried, and the ether removed (cf. Salomon, *J. pr. Chem.*, 1872, **6**, 445). The crude oils were used directly in the next step.

The following illustrates the general procedure for the final step. N-*Thioncarbethoxyglycine* (XIV; R = Et). Ethyl ethoxydithioformate (75 g., 0·5 mol.) in alcohol (50 c.c.) was added to a solution of

potassium hydroxide (28 g., 0·5 mol.) and glycine (37·5 g., 0·5 mol.) in water (50 c.c.), and the whole refluxed on the steam-bath for 18 hours, the ethanethiol being allowed to distil off. Water (50 c.c.) was added, and the solution clarified by ether-extraction, concentrated to half volume, and acidified with cold concentrated hydrochloric acid (50 c.c.). The required *ester* (55·5 g., 68%) separated and formed glassy needles, m. p. 101°, from water (Found: C, 37·0; H, 5·0; N, 8·2; S, 19·65. $C_5H_9O_2NS$ requires C, 36·8; H, 5·5; N, 8·6; S, 19·9%).

The esters recorded in Table II were obtained in a similar manner.

2-Alkoxythiazol-5-ones.—*N*-Thioncarbalkoxyglycine (10 g.) and acetic anhydride (50 c.c.) were heated for 30 minutes in an oil-bath at 130°, and the solvents removed under reduced pressure. The residual oils were used directly in dye formation. *E.g.*, *N*-thioncarbethoxyglycine (10 g.) and acetic anhydride (50 c.c.) gave an oil which on distillation gave a colourless oil, b. p. 57°/4 mm. (62°/5 mm.), which became light brown on storage (Found: N, 7·65; S, 18·6. $C_5H_7O_2NS$ requires N, 9·65; S, 22·1%). It gave the same dyes as the crude reaction mixture and appears to be the required *2-ethoxythiazol-5-one* contaminated with acetic anhydride.

TABLE II.

R in (XIV).	Appearance.	M. p.	Solvent.*	Formula.	Found, S, %.	Reqd., S, %.
iso*Propyl*	Long, flat needles	129°	Water	$C_6H_{11}O_2NS$	18·1	18·1
n-*Butyl*	Glossy needles	70—71	,,	$C_7H_{13}O_2NS$	16·95	16·75
n-*Amyl*	Needles	49—50	Light petroleum	$C_8H_{15}O_2NS$	15·75	15·6
tert.-*Amyl* ...	Fine threads	52—54	,,	,,	15·75	,,
n-*Hexyl*	Small needles	62	,,	$C_9H_{17}O_2NS$	6·25 (N)	6·4 (N)
n-*Heptyl*	,,	66	,,	$C_{10}H_{19}O_2NS$	6·15 (N)	6·0 (N)
n-*Octyl*	Fine needles	72	,,	$C_{11}H_{21}O_2NS$	5·8 (N)	5·65 (N)
n-*Decyl*	Glistening plates	63	,,	$C_{13}H_{25}O_2NS$	11·55	11·65
n-*Dodecyl*	Fine needles	67	,,	$C_{15}H_{29}O_2NS$	4·85 (N)	4·6 (N)
n-*Tetradecyl* ...	,,	79	,,	$C_{17}H_{33}O_2NS$	9·5	9·65
n-*Hexadecyl* ...	,,	77	,,	$C_{19}H_{37}O_2NS$	4·05 (N)	3·9 (N)
3-*Phenylpropyl*	Asbestos-like threads	88	Benzene–light petroleum	$C_{12}H_{15}O_2NS$	12·5	12·65

* Light petroleum had b. p. 60—80°.

4-Ethoxymethylene-2-alkoxythiazol-5-ones.—The *N*-thiocarbalkoxyglycine (0·01 mol.), acetic anhydride (10 c.c.), and ethyl orthoformate (3·5 c.c.) were heated in an oil-bath at 135—140° for 30 minutes, the alcohol being allowed to distil off. Removal of the solvents under reduced pressure left an oil which usually crystallised on chilling. The crude products were used directly in dye formation. The following were characterised:

2-n-*Decyloxy-4-ethoxymethylenethiazol-5-one*, pale yellow needles, m. p. 50°, from ethanol (Found: N, 4·4. $C_{16}H_{27}O_3NS$ requires N, 4·45%); 2-n-*dodecyloxy-4-ethoxymethylenethiazol-5-one*, pale yellow needles, m. p. 58°, from ethanol (Found: N, 4·1. $C_{18}H_{31}O_3NS$ requires N, 4·1%); *4-ethoxymethylene-2-n-tetradecyloxythiazol-5-one*, soft, pale yellow needles, m. p. 64°, from ethanol (Found: C, 65·1; H, 9·25; N, 3·5; S, 8·65. $C_{20}H_{35}O_3NS$ requires C, 65·0; H, 9·5; N, 3·8; S, 8·7%).

N-(NN-*diethylthiocarbamyl*)*glycine* (XIX; R = R′ = Et).—Potassium hydroxide (6·24 g.) was dissolved in water (20 c.c.), *N*-dithiocarbethoxyglycine (20 g.) and diethylamine (11·8 c.c.) were added, and the whole was refluxed for 15 hours. After cooling, the solution was extracted with ether, and the aqueous layer cautiously acidified with concentrated hydrochloric acid. After chilling and scratching, crystallisation set in. The solid (11·0 g., 52%) after air-drying formed small, buff-coloured crystals, m. p. 105°, from benzene (Found: N, 14·4; S, 16·8. $C_7H_{14}O_2N_2S$ requires N, 14·7; S, 16·85%).

N-(N-*Methyl*-N-*phenylthiocarbamyl*)*glycine* (XIX; R = Ph, R′ = Et).—Potassium hydroxide (3·12 g.) and *N*-dithiocarbethoxyglycine (10 g.) were dissolved in water (16 c.c.) and ethanol (32 c.c.), and after the addition of *N*-ethylaniline (6·8 g.) the whole was refluxed 24 hours on the steam-bath. Water (50 c.c.) was added and the mixture extracted with ether. The aqueous layer was acidified with concentrated hydrochloric acid and the *amide* collected after chilling. It (3·05 g., 21%) formed a buff-coloured crystalline powder, m. p. 138°, from water (Found: N, 11·8. $C_{11}H_{14}O_2N_2S$ requires N, 12·0%).

1-N′-*Carboxymethylthiocarbamylpiperidine* (XXI).—Potassium hydroxide (18·72 g.) and *N*-dithiocarbethoxyglycine (60 g.) were dissolved in water (250 c.c.), to this solution was added piperidine (28·5 g.), and the mixture refluxed for 24 hours. Acidification of the chilled solution gave a bulky precipitate of the *glycine* derivative as a hydrate (18·5 g., 22·6%) which formed colourless needles, m. p. 171°, from water (Found: N, 12·9; S, 14·3. $C_8H_{14}O_2N_2S,H_2O$ requires N, 12·6; S, 14·55%).

4-N′-*Carboxymethylthiocarbamylmorpholine* (XXII).—Obtained similarly from morpholine (29·2 g.), this formed a *hydrate*, colourless needles, m. p. 171° (49·5% yield), from water (Found: N, 12·3; S, 14·2. $C_7H_{12}O_3N_2S,H_2O$ requires N, 12·6; S, 14·4%).

The 2-*tert.*-aminothiazol-5-one hydrobromides were obtained as oils on addition of phosphorus tribromide (1 c.c.) to the above glycines (2 g.) dissolved in dioxan (15 c.c.) and anhydrous ether (45 c.c.). The oils were washed with ether and used directly in the dye condensations.

*Dimethin*merocyanines.¶—The *dyes* recorded in Tables III and IV were prepared by treating, for 5—10 minutes on the steam-bath, an alcoholic solution of triethylamine (1 mol.) and (*a*) the 2-acetanilidovinyl derivative of the required cyclic ammonium salt (1 mol.) with the keto-methylene heterocyclic compound (II) (1 mol.) or (*b*) the reactive methyl derivative of the same ammonium salt (1 mol.) with the 4-ethoxymethylene (or 4-1′-ethoxyethylidene) derivative (III) (1 mol.). When the hydrobromides of the latter were employed two mols. of triethylamine were added.

TABLE III.

Ref. no.	[Heterocyclic nucleus][4-(2-phenyloxazol-5-one)] dimethin*mero*cyanine.	Appearance.	M. p.	S.‡	Formula.	Found, N, %.	Reqd., N, %.
1	[2-(1-Ethylquinoline)] *	Green plates	227°	BL	$C_{33}H_{19}O_2N$	7·85	8·2
2	[2-(3-Ethylbenzoxazole)] *	Red needles	225	BL	$C_{20}H_{16}O_3N_2$	8·35	8·45
3	[2-(3-Ethylbenzothiazole)] *	,,	209 †	BL	$C_{20}H_{16}O_2N_2S$	7·75	8·05
4	[2-(3-Ethylbenzoselenazole)].....	Magenta needles	222	BL	$C_{20}H_{16}O_2N_2Se$	6·8	7·1
5	[2-(1 : 3 : 3-Trimethylindolenine)]	Red needles	198	BL	$C_{22}H_{20}O_2N_2$	7·5	8·15
6	[4-(1-Ethylquinoline)]	Green needles	212	BL	$C_{33}H_{19}O_2N_2$	7·85	8·2
7	[2-(3-Methylthiazoline)] *	Brick-red crystals	212	M	$C_{15}H_{14}O_2N_2S$	9·9	9·8
8	[2-(3-Ethyl-4-methylthiazole)] ...	Steel-grey crystals	209	BL	$C_{17}H_{16}O_2N_2S$	9·05	9·0
9	[2-(3-Methylnaphtho-1′ : 2′-4 : 5-oxazole)]	Red needles	288	PW	$C_{23}H_{16}O_2N_2$	7·2	7·6
10	[2-(3-Ethylnaphtho-2′ : 1′-4 : 5-oxazole)]	,,	250	B	$C_{24}H_{18}O_2N_2$	7·35	7·35
11	[2-(3-Ethylnaphtho-1′ : 2′-4 : 5-thiazole)]	Purple needles	206	B	$C_{24}H_{18}O_2N_2S$	7·0	7·05
12	[2-(3-Ethylnaphtho-2′ : 1′-4 : 5-thiazole)]	,,	260	PW	,,	7·0	7·05
13	[2-(1-Ethyl-7 : 8-benzoquinoline)]	Green needles	139	BL	$C_{24}H_{20}O_2N,C_6H_6$	6·0	5·95
14	[2-(3-Ethyl-4-*p*-methoxyphenylthiazole)]	Red needles	180	B	$C_{23}H_{20}O_2N_2S$	6·8	6·95

* Obtained by Keyes and Brooker (*loc. cit.*). † Cook *et al.*, *loc. cit.*, give m. p. 210°.
‡ Solvent: B = benzene; C = chloroform; E = ethanol; L = light petroleum (b. p. 40—60°); M = methanol; P = pyridine; W = water.

TABLE IV.

Ref. no.	[α-(Heterocyclic nucleus][β-4(2-phenyloxazol-5-one)]-β-methyldimethin*mero*cyanine.	Appearance.	M. p.	S.*	Formula.	Found, N, %.	Reqd., N, %.
15	[α-2-(1-Ethylquinoline)]	Flat, green needles	198°	BL	$C_{33}H_{20}O_2N_2$	7·55	7·85
16	[α-2-(3-Methylthiazoline)]	Brick-red crystals	210	BL	$C_{16}H_{16}O_2N_2S$	9·1	9·35
17	[α-2-(3-Ethylbenzoxazole)]	Orange needles	209	BL	$C_{21}H_{18}O_3N_2$	7·7	8·1
18	[α-2-(3-Ethylbenzothiazole)].....	Red needles	237	B	$C_{21}H_{18}O_2N_2S$	7·9	7·75
19	[α-2-(3-Ethylbenzoselenazole)]	Violet needles	228	B	$C_{21}H_{18}O_2N_2Se$	6·95	6·85
20	[α-2-(3-Ethyl-4-methylthiazole)] ...	Purple needles	232	B	$C_{18}H_{18}O_2N_2S$	8·9	8·6

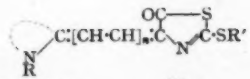
* See footnote, table III.

*Dimethin*merocyanines (cf. Table V) containing the 2-alkylthiothiazol-5-one nuclei were obtained similarly. *mero*Cyanines were also obtained by the standard procedure of treating the thiazolone (II) with the 2-methylthio-derivative of the cyclic ammonium salt in alcoholic triethylamine. *Tetramethin*merocyanines (Table V) were obtained similarly by using the 4-acetanilidobuta-1 : 3-dienyl derivatives of the cyclic ammonium salt.

[α-2-(3-*Ethylbenzoxazole*)][β-4-(2-*n*-*decylthiothiazol*-5-*one*)]-β-*methyldimethin*merocyanine.—*N*-Dithiocarbo-*n*-decyloxyglycine (1·45 g.), acetic anhydride (15 c.c.), and ethyl orthoacetate (6 c.c.) were heated

¶ In the naming of the dyes the ketonic nucleus is placed in the second bracket irrespective of the alphabetical order of the two nuclei. The nucleus in the first bracket, which is actually a dihydro-derivative of the heterocyclic nucleus, is simplified in all cases. Thus 3-ethylbenzothiazoline is called 3-ethylbenzothiazole, 3-ethylthiazolidine is called 3-ethylthiazoline, etc., as the termination *mero*cyanine indicates the structure. Hamer and Winton (*J.*, 1949, 1126) use both forms. The first dye in Table III is thus [2-(1-ethylquinoline)][4-(2-phenyloxazol-5-one)]dimethin*mero*cyanine.

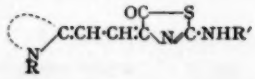
TABLE V.



Ref. no.	Heterocyclic group.	R′.	Appearance.	M. p.	S.‡	Formula.	Found, N, %.	Reqd., N, %.
	[*Heterocyclic group*][4-(2-*alkylthiothiazol*-5-*one*)]*dimethin*merocyanine.							
21	[2-(3-Ethylbenzoxazole)]	H	Yellow prisms	232°	B	$C_{14}H_{12}O_2N_2S_2$	9·1	9·2
22	[2-(3-Ethylbenzothiazole)]	,,	Brown crystals	236	B	$C_{14}H_{12}ON_2S_3$	8·7	8·75
23	[2-(1-Ethylquinoline)]	,,	Black powder	232	B	$C_{16}H_{14}ON_2S_2$	8·65	8·65
24	[2-(3-Ethylbenzoxazole)]	Et	Flat, steel blue needles	156	E	$C_{16}H_{16}O_2N_2S_2$	8·4	8·45
25	[2-(3-Ethylbenzothiazole)] *	,,	Blue-grey prisms	173	B	$C_{16}H_{16}ON_2S_3$	8·2	8·05
26	[2-(3-Ethylbenzoselenazole)]	,,	,,	184	B	$C_{16}H_{16}ON_2S_2Se$	7·05	7·1
27	[2-(3-Methylthiazoline)]	,,	Maroon needles	139	E	$C_{11}H_{14}ON_2S_2$	9·6	9·8
28	[2-(3-Ethylthiazoline)]	,,	Yellow plates	121	E	$C_{12}H_{16}ON_2S_2$	10·75 †	10·65 †
29	[2-(3-Ethyl-4-methylthiazole)]	,,	Green prisms	154	E	$C_{12}H_{14}ON_2S_2$	9·1	9·0
30	[2-(4-*p*-Methoxyphenyl-3-ethylthiazole)]	,,	Maroon needles	182	B	$C_{19}H_{18}O_2N_2S_2$	6·75	6·95
31	[2-(3-Ethylnaphtho-1′ : 2′-4 : 5-thiazole)]	,,	,,	172	B	$C_{20}H_{16}ON_2S_2$	7·1	7·05
32	[2-(1-Ethylquinoline)]	,,	Green needles	163	BE	$C_{18}H_{18}ON_2S_2$	8·4	8·2
33	[4-(1-Ethylquinoline)]	,,	Blue plates	143	E	,,	8·1	8·2
34	[2-(1 : 3 : 3-Trimethylindolenine)]	,,	Red needles	137	BE	$C_{18}H_{20}ON_2S_2$	8·1	8·15
35	[2-(3-Ethylbenzoxazole)]	CH_2Ph	Orange needles	193	E	$C_{20}H_{16}O_2N_2S_2$	7·05	7·1
36	[2-(3-Ethylbenzothiazole)] *	,,	Red needles	179	E	$C_{21}H_{16}ON_2S_3$	6·4	6·85
37	[2-(3-Ethylbenzoselenazole)]	,,	Violet needles	165	E	$C_{21}H_{16}ON_2S_2Se$	5·95	6·1
38	[2-(3-Ethylnaphtho-1′ : 2′-4 : 5-thiazole)]	,,	Purple needles	215	BE	$C_{25}H_{20}ON_2S_3$	5·9	6·0
39	[2-(3-Methylthiazoline)]	,,	Red-green prisms	171	BE	$C_{16}H_{16}ON_2S_2$	7·95	8·05
40	[2-(1-Ethylquinoline)]	,,	Green needles	207	E	$C_{23}H_{20}ON_2S_2$	6·55	6·95
41	[4-(1-Ethylquinoline)]	,,	Blue needles	162	E	$C_{23}H_{20}ON_2S_2$	6·75	6·95
42	[2-(1-Ethylpyridine)]	,,	Purple needles	152	E	$C_{19}H_{18}ON_2S_2$	7·8	7·9
43	[4-(1-Methylpyridine)]	,,	Green crystals	172	E	$C_{18}H_{16}ON_2S_2$	7·9	8·25
44	[2-(3-Methylthiazoline)]	$CH_2{\cdot}C_6H_4{\cdot}NO_2$-*p*	Bronze plates	202	PE	$C_{16}H_{15}O_3N_3S_2$	10·45	10·7
45	[2-(3-Ethylbenzoxazole)]	,,	Purple needles	201	PE	$C_{21}H_{17}O_4N_3S_2$	9·2	9·6
46	[2-(3-Methylthiazoline)]	$CH_2{\cdot}C_6H_4{\cdot}NO_2$-*m*	Steel-blue plates	187	PE	$C_{16}H_{15}O_4N_3S_2$	10·7	10·7
47	[2-(3-Ethylbenzothiazole)]	,,	Green needles	178	PE	$C_{21}H_{17}O_3N_3S_2$	9·4	9·25
48	[2-(3-Ethylbenzoxazole)]	,,	Red crystals	192	PE	$C_{21}H_{17}O_4N_3S_2$	9·4	9·6
49	[2-(3-Ethylbenzoxazole)]	C_6H_{13}-*n*	Red-brown platelets	148	E	$C_{20}H_{24}O_2N_2S_2$	16·6 †	16·5 †
50	,,	C_7H_{15}-*n*	Rust-red crystals	133	E	$C_{21}H_{26}O_2N_2S_2$	15·4 †	15·9 †
51	[2-(3-Ethylbenzoselenazole)]	,,	Glassy, violet needles	112	E	$C_{21}H_{26}ON_2S_2Se$	6·1	6·05
52	[2-(3-Methylthiazoline)]	C_8H_{17}-*n*	Purple needles	81	E	$C_{17}H_{26}ON_2S_2$	26·3 †	25·95 †
53	[2-(3-Ethylthiazoline)]	,,	Orange crystals	86	E	$C_{18}H_{28}ON_2S_2$	25·25 †	25·0 †
54	[2-(3-Ethylbenzoxazole)]	,,	Glossy orange crystals	130	E	$C_{23}H_{28}O_2N_2S_2$	6·75	6·75
55	[2-(3-Ethylbenzothiazole)]	,,	Red needles	81	BM	$C_{23}H_{28}ON_2S_3$	22·2 †	22·2 †
56	[2-(3-Ethyl-5-chlorobenzothiazole)]	,,	Purple needles	156	B	$C_{23}H_{27}ON_2ClS_3$	20·3 †	20·6 †
57	[2-(3-Ethylbenzoselenazole)]	,,	Violet needles	88	BM	$C_{23}H_{28}ON_2S_2Se$	6·05	5·85
58	[2-(3-Ethylbenzoxazole)]	$C_{10}H_{21}$-*n*	Orange powder	106	E	$C_{24}H_{32}O_2N_2S_2$	5·95	6·2
59	,,	$C_{13}H_{25}$-*n*	Rust powder	103	M	$C_{27}H_{38}O_2N_2S_2$	13·55	13·55
60	,,	$[CH_2]_3{\cdot}Ph$	Red prisms	170	E	$C_{22}H_{22}O_2N_2S_2$	15·05 †	15·2 †
	[*Heterocyclic group*][4-(2-*alkylthiothiazol*-5-*one*)]merocyanine (n = 0).							
61	[2-(1-Methylquinoline)]	CH_2Ph	Dark-green crystals	144	BL	$C_{20}H_{16}ON_2S_2$	7·75	7·7
62	[2-(3-Methylbenzothiazole)]	,,	Yellow needles	193	BL	$C_{18}H_{14}ON_2S_3$	7·45	7·55
	[*Heterocyclic group*][4-(2-*alkylthiothiazol*-5-*one*)]*tetramethin*merocyanine (n = 2).							
63	[2-(3-Ethylbenzothiazole)]	Et	Blue crystals	179	E	$C_{18}H_{16}ON_2S_3$	25·8 †	25·65 †

* See also Cook *et al.* (*loc. cit.*). † Sulphur (not nitrogen). ‡ See footnote to Table III.

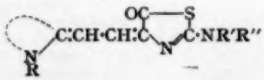
TABLE VI.



Ref. no.	[(Heterocyclic group)][4-(2-acylamidothiazol-5-one)]dimethin-*mero*cyanine.	R′.	Appearance.	M. p.	S‡.	Formula.	Found, N, %.	Reqd., N, %.
64	[2-(1-Ethylquinoline)]	COMe	Green needles	253°	B	$C_{16}H_{17}O_2N_3S$	12·35	12·4
65	[4-(1-Ethylquinoline)]	,,	Green powder	226	E	,,	12·1	12·4
66	[2-(3-Ethylbenzoxazole)]	,,	Red needles	264	C	$C_{16}H_{15}O_2N_3S$	12·8	12·75
67	[2-(3-Ethylbenzothiazole)]	,,	Green-brown needles	228	B	$C_{16}H_{15}O_2N_3S_2$	12·3	12·15
68	[2-(3-Ethylthiazoline)]	,,	Orange crystals	252	B	$C_{12}H_{13}O_2N_3S_2$	14·05	14·15
69	[2-(3-Ethylbenzoselenazole)]	,,	Green crystals	239	C	$C_{16}H_{15}O_2N_3SSe$	10·7	10·7
70	[2-(3-Ethylbenzoxazole)]	COPr^n	Brick-red needles	212	E	$C_{18}H_{19}O_2N_3S$	12·1	11·75
71	[2-(3-Methylthiazoline)]	,,	Orange prisms	229	M	$C_{12}H_{17}O_2N_3S$	13·4	13·5
72	[2-(3-Ethylbenzoxazole)]	COPh	Brick-red needles	262	E	$C_{21}H_{17}O_2N_3S$	10·6	10·75
73	[2-(3-Methylthiazoline)]	,,	Orange needles	242	E	$C_{16}H_{15}O_2N_3S$	11·9	12·2

‡ See footnote to Table III.

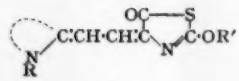
TABLE VIII.



Ref. no.	[(Heterocyclic group)][4-(2-*tert.*-aminothiazol-5-one)]dimethin-*mero*cyanine.	NR′R″.	Appearance.	M. p.	S.‡	Formula.	Found, N, %.	Reqd., N, %.
102	[2-(1-Ethylquinoline)]	NEt_2	Green needles	158°	E	$C_{20}H_{22}ON_2S$	11·2	11·7
103	[4-(1-Ethylquinoline)]	,,	Green crystals, golden reflex	163	E	,,	11·6	11·7
104	[2-(3-Ethylbenzoxazole)]	,,	Brick-red needles	163	E	$C_{16}H_{21}O_2N_3S$	12·3	12·2
105	[2-(3-Ethylbenzothiazole)]	,,	Maroon plates	156	E	$C_{16}H_{21}ON_3S_2$	9·2	9·3
106	[2-(3-Ethylbenzoselenazole)]	,,	Orange-red crystals	153	E	$C_{16}H_{21}ON_3SSe$	10·1	10·3
107	[2-(3-Ethyl-naphtho-1′ : 2′-4 : 5-thiazole)]	,,	Maroon needles	167	E	$C_{20}H_{23}ON_3S_2$	9·8	10·2
108	[2-(3-Ethyl-4-methylthiazole)]	,,	Green needles	158	E	$C_{16}H_{21}ON_3S_2$	13·0	13·0
109	[2-(3-Ethylthiazoline)]	,,	Orange prisms	118	EW	$C_{16}H_{21}ON_3S_2,H_2O$	12·8	12·9
110	[2-(1 : 3 : 3-Trimethylindolenine)]	,,	Red plates, golden reflex	167	E	$C_{20}H_{23}ON_3S$	11·7	11·8
111	[2-(3-Ethylbenzoxazole)]	NPhEt	Orange prisms	183	E	$C_{22}H_{21}O_2N_3S$	10·6	10·7
112	[2-(3-Ethylbenzothiazole)]	,,	Brick-red plates	178	E	$C_{22}H_{21}ON_3S_2$	10·2	10·3
113	[2-(3-Ethylbenzoxazole)]	$N<[CH_2]_5$	Brick-red prisms	192	E	$C_{19}H_{21}O_2N_3S$	12·1	11·8
114	[2-(3-Ethylbenzothiazole)]	,,	Maroon plates	155	E	$C_{19}H_{21}ON_3S_2$	11·5	11·35
115	[2-(3-Ethylbenzoxazole)]	$N<([CH_2]_2)_2O$	Orange powder	218	E	$C_{18}H_{19}O_3N_3S$	11·6	11·7

‡ See footnote to Table III.

TABLE VII.



Ref. no.	[(Heterocyclic group)][4-(2-alkoxythiazol-5-one)]dimethin*mero*cyanine.	R′.	Appearance.	M. p.	S.‡	Formula.	Found, N, %.	Reqd., N, %.
74	[2-(3-Methylthiazoline)]	Et	Brown needles	209°	B	$C_{11}H_{16}O_2N_2S_2$	10·3 23·65 •	10·35 23·7 •
75	[2-(3-Ethylthiazoline)]	,,	Orange needles	136	E	$C_{12}H_{18}O_2N_2S_2$	9·8	9·85
76	[2-(1 : 3 : 3-Trimethylindolenine)]	,,	Glossy, red plates	170	M	$C_{18}H_{20}N_2S$	8·5	8·55
77	[2-(1-Ethylquinoline)]	,,	Blue needles	145	M	$C_{16}H_{16}O_2N_2S$	8·4	8·1
78	[4-(1-Ethylquinoline)]	,,	Grey-green crystals	183	M	,,	8·2	8·1
79	[2-(3-Ethylbenzoxazole)]	,,	Golden plates or hard prisms	192	E	$C_{16}H_{16}O_2N_2S$	8·2	8·35
80	[2-(3-Ethylbenzothiazole)]	,,	Violet needles	188	E	$C_{16}H_{16}O_2N_2S$	7·6	7·95
81	[2-(3-Ethylbenzoselenazole)]	,,	Garnet needles	192	B	$C_{16}H_{16}O_2N_2SSe$	7·05	7·05
82	[2-(3-Ethylnaphtho-1′ : 2′-4 : 5-thiazole)]	,,	Purple needles	202	B	$C_{20}H_{18}O_2N_2S_2$	7·6	7·35
83	[2-(3-Ethylnaphtho-1′ : 2′-4 : 5-oxazole)]	,,	Orange needles	248	E	$C_{20}H_{18}O_3N_2S$	7·6	7·65
84	[2-(3-Ethyl-4-methylthiazole)]	,,	Garnet plates	173	E	$C_{12}H_{16}O_2N_2S_2$	9·2	9·45
85	[2-(3-Ethylbenzoxazole)]	Pr^i	Orange needles	184	E	$C_{17}H_{18}O_2N_2S$	8·35	8·5
86	[2-(3-Methylthiazoline)]	,,	Flat, brown needles, blue reflex	180	E	$C_{12}H_{16}O_2N_2S_2$	9·75	10·0
87	[2-(3-Ethylbenzothiazole)]	,,	Red needles	163	E	$C_{17}H_{18}O_2N_2S_2$	8·15	8·1
88	[2-(3-Ethylbenzoxazole)]	Bu^n	Orange needles	150	M	$C_{18}H_{20}O_2N_2S$	8·4	8·15
89	[2-(3-Methylthiazoline)]	,,	Flat, brown needles, blue reflex	172	E	$C_{12}H_{16}O_2N_2S$	9·35	9·4
90	[2-(3-Methylthiazoline)]	n-C_5H_{11}	Flat, brown needles, blue reflex	128	M	$C_{14}H_{20}O_2N_2S_2$	9·3	9·0
91	,,	*tert.*-C_5H_{11}	Flat, red-brown platelets	136—138	E	$C_{14}H_{20}O_2N_2S_2$	9·35	9·0
92	,,	n-C_6H_{13}	Yellow powder	117	E	$C_{15}H_{22}O_2N_2S_2$	8·5	8·6
93	,,	n-C_7H_{15}	Orange cryst.	115	E	$C_{16}H_{24}O_2N_2S_2$	8·45	8·25
94	[4-(1-Ethylquinoline)]	,,	Black plates	111	E	$C_{23}H_{28}O_2N_2S$	6·75	7·05
95	[2-(3-Methylthiazoline)]	n-C_8H_{17}	Flat, yellow needles	114—116	M	$C_{17}H_{26}O_2N_2S_2$	8·1	7·9
96	[2-(3-Ethylbenzoselenazole)]	,,	Red needles	138	E	$C_{23}H_{28}O_2N_2SSe$	6·2	6·05
97	[2-(3-Methylthiazoline)]	n-$C_{10}H_{21}$	Orange powder	115	E	$C_{19}H_{30}O_2N_2S_2$	7·3	7·35
98	,,	n-$C_{12}H_{25}$	Yellow powder	111	E	$C_{21}H_{34}O_2N_2S_2$	7·05	6·85
99	,,	n-$C_{14}H_{29}$	Glistening, yellow cryst.	117	E	$C_{23}H_{38}O_2N_2S_2$	6·35	6·4
100	,,	n-$C_{16}H_{33}$	Gold yellow crystals	106—107	E	$C_{25}H_{42}O_2N_2S_2$	5·7	6·0
101	,,	$[CH_2]_3$·Ph	Flat, brown needles	159	E	$C_{16}H_{20}O_2N_2S_2$	7·85	7·8

• Sulphur (not nitrogen).

‡ See footnote to Table III.

together in an oil-bath at 120° for 30 minutes. The solvents were removed under reduced pressure, 2-methylbenzoxazole ethiodide (1·45 g.), ethanol (10 c.c.), and triethylamine (1 c.c.) were added, and the whole was heated for 5 minutes on the steam-bath. The solvent was boiled off and the residue scratched to start crystallisation. The triethylamine hydriodide was removed with a little cold methanol, and the *dye* was then obtained as soft, orange needles, m. p. 68°, from ethanol (Found: N, 5·95. $C_{31}H_{34}O_3N_2S_3$ requires N, 6·1%). The *β-ethyl* homologue was similarly obtained by using orthopropionate and formed soft, orange needles, m. p. 96°, from ethanol (Found: N, 6·25. $C_{34}H_{36}O_3N_2S_3$ requires N, 5·95%).

[α-2-(3-*Ethylnaphtho*-1′ : 2′-4 : 5-*thiazole*)][β-4-(2-*ethylthiothiazol*-5-*one*)] 3-*methyldimethinmerocyanine* was similarly obtained, formed violet needles, m. p. 209°, from benzene (Found: N, 6·8. $C_{21}H_{20}ON_2S_3$ requires N, 6·8%), and had an absorption max. at 540 mμ. in methanol.

Absorption Data.—These are recorded below.

Ref. no.	$\lambda_{max.}$	Ref. no.	$\lambda_{max.}$	Ref. no.	$\lambda_{max.}$	Ref. no.	$\lambda_{max.}$	Ref. no.	$\lambda_{max.}$
1	538 (567i)	24	500 (474i)	47	530 (505i)	70	489 (472i)	93	444
2	492	25	527 (500i)	48	492 (475i)	71	476 (464)	94	568
3	522 (493i)	26	528 (505i)	49	494 (463i)	72	498 (478i)	95	444
4	525 (495i)	27	463 (448)	50	491 (465i)	73	486 (468)	96	500
5	492 (465i)	28	470	51	532 (510i)	74	445	97	445
6	620 (580)	29	528 (502i)	52	478 (463)	75	452	98	444
7	474 (450)	30	530 (505i)	53	479 (464)	76	473	99	445
8	530 (502i)	31	548 (515i)	54	489 (465i)	77	530 (500i)	100	444
9	506	32	546	55	529 (498i)	78	568 (607)	101	445
10	506	33	591 (620i)	56	528 (498i)	79	460	102	560
11	529	34	500 (490)	57	531 (500)	80	499	103	588
12	539 (506i)	35	490 (476i)	58	492 (472i)	81	505	104	480
13	531 (505)	36	530 (508i)	59	490 (476i)	82	541	105	519
14	531 (505)	37	531 (508i)	60	492 (470i)	83	485	106	517
15	566	38	545 (520i)	61	485	84	518	107	560
16	475 (455)	39	472 (462)	62	400	85	467	108	542
17	490 (462i)	40	549	63	640 (596i)	86	446	109	469
18	515 (495i)	41	593 (620i)	64	555 (600)	87	494	110	481
19	518 (492i)	42	510	65	593 (630)	88	469	111	482
20	514 (484i)	43	533	66	488 (462i)	89	450	112	518
21	493	44	478 (460)	67	528 (500i)	90	440	113	480
22	522	45	493 (470i)	68	480 (464)	91	443	114	519
23	551 (582i)	46	478 (465)	69	528 (500i)	92	444	115	479

The authors are indebted to Miss M. E. Cole and Miss E. M. Hamilton for the preparation of some of the intermediates.

RESEARCH LABORATORIES, KODAK LIMITED, WEALDSTONE, MIDDLESEX.
VEI 2961, SMESTAD, OSLO, NORWAY. [*Received, March 15th*, 1951.]

---

477. *Thiazolid-2 : 5-dione.*

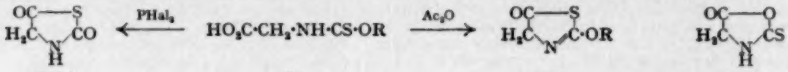
By PER AUBERT, R. A. JEFFREYS, and E. B. KNOTT.

It is shown that the product obtained by treating *N*-thioncarbethoxyglycine (I) (see previous paper) with phosphorus trihalides is thiazolid-2 : 5-dione (III). It is also obtained by the dealkylation of 2-ethoxythiazol-5-one with phosphorus trihalides in moist benzene. It readily polymerises on heating its aqueous solution to give what is believed to be a polyglycine. The attempted cyclodealkylation of *N*-thiocarbethoxysarcosine (VI) and *N*-thiocarbethoxy-DL-alanine (VII) did not give solid reaction products.

IN the preceding paper it was observed that whereas the cyclodehydration of *N*-thiocarbethoxyglycine (I; R = Et) with acetic anhydride gave the expected 2-ethoxythiazol-5-one (II; R = Et), treatment of (I; R = Et) with phosphorus trihalides gave a product which was not the expected hydrobromide of (II; R = Et). This behaviour was unexpected in that, as Cook, Harris, Heilbron, and Shaw (*J.*, 1949, 1056) have shown, the related *N*-dithiocarbobenzyloxyglycine readily gives 2-benzylthiothiazol-5-one hydrobromide on treatment with phosphorus tribromide.

That the reaction involved the loss of the alkyl group (R) was shown by the fact that the same product resulted from (I) irrespective of the nature of R. It could be recrystallised from water in inch-long laths, m. p. 110°, but if the solution was heated for too long or at too high a temperature an inflammable gas was evolved which had the odour of hydrogen sulphide and

contained labile sulphur. Prolonged heating in dilute solution, or shorter heating in more concentrated solution, resulted in the precipitation of an insoluble white powder containing



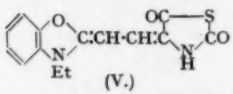
(III.) (I.) (II.) (IV.)

nitrogen and a trace of sulphur. It dissolved in aqueous sodium carbonate with evolution of carbon dioxide. The presence of a reactive methylene group was indicated by the development of colour with triethylamine–alcohol solutions of 2-acetanilidovinyl derivatives of heterocyclic quaternary salts.

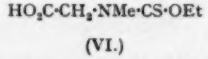
Analysis indicated an empirical formula $C_3H_3O_2NS$ (no halogen) which corresponds to loss of a molecule of water from the acid (I; R = H). The substance was thus formulated as thiazolid-2 : 5-dione (III) or (since ethyl chloride may be eliminated from the intermediate acid chloride) 2-thio-oxazolid-5-one (IV).* The preferential formation of an oxazolidine ring seemed, however, unlikely. Proof of the correctness of the formulation (III) was then obtained by dealkylation of 2-ethoxythiazol-5-one (II; R = Et) by phosphorus trihalides in moist benzene giving, in high yield, the identical product of m. p. 110°. This ready loss of the alkyl group, presumably by acid hydrolysis, appears to be analogous to the formation of 2-hydroxythiazoles instead of the expected ethers on condensation of ethyl thioncarbamates with α-halogeno-ketones (Hantzsch and Hubacher, *Annalen*, 1890, **259**, 250; Knott, *J.*, 1947, 1656).

The synthesis of this compound has been attempted by Cook, Heilbron, and Hunter (*J.*, 1949, 1443), who thought that it might possess a stability intermediate between that of oxazolid-2 : 5-dione (anhydro-*N*-carboxyglycine) and 2-thiothiazolid-5-one and would thus be a more useful reagent than either of these compounds. Although (III) has not been exploited at all fully it would appear that their expectation is realized in that it is fairly stable (when pure) towards moist air and yet readily polymerises on heating. It gives salt-like compounds on treatment with morpholine or triethylamine which may be analogous to the products obtained by Cook and Levy (*J.*, 1950, 646) from 2-thiothiazolid-5-one.

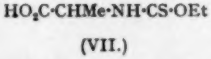
The condensation of (III) with 2-2′-acetanilidovinylbenzoxazole ethiodide in boiling alcoholic triethylamine gave a dye, the magenta solutions of which in methanol slowly faded. Analysis indicated an empirical formula of $C_{16}H_{18}O_4N_2S$ which corresponds to the addition of a molecule of ethanol to the expected [2-(3-ethylbenzoxazole)] [4-thiazolid-2 : 5-dione)]dimethin*mero*-cyanine (V). The latter dye, giving yellow solutions in methanol, was obtained by the cold reaction of the above components.



(V.)



(VI.)



(VII.)

The condensation of ethyl ethoxydithioformate with sarcosine and DL-alanine gave *N*-thioncarbethoxysarcosine (VI) and *N*-thioncarbethoxy-DL-alanine respectively. Attempts to effect cyclodealkylation of these compounds gave oils which have not been investigated.

Experimental.

Analyses are by Drs. Weiler and Strauss, Oxford.

Thiazolid-2 : 5-dione (III).—(*a*) *N*-Thioncarbethoxyglycine (5 g.) (preceding paper) was covered with benzene (15 c.c.), and phosphorus trichloride (3 c.c., 1·1 mols.) was added. The flask was warmed gently on the steam-bath until the glycine commenced to liquefy. The flask was swirled until the contents were completely molten (*ca.* 40°). Crystallisation then set in rapidly. The solid *dione* was collected immediately (if it is left overnight some liquefaction occurs) and washed with benzene, then ice-cold water (20 c.c.) to remove a slight stickiness. The colourless crystals (2·7 g., 75%) were dissolved cautiously in the minimum of warm water and chilled. Long laths, m. p. 110°, separated. Alternatively small crystals were obtained by ice-cooling of its alcoholic solution (Found: C, 31·2; H, 2·65; N, 11·6; S, 27·1. $C_3H_3O_2NS$ requires C, 30·75; H, 2·55; N, 11·95; S, 27·4%). The yield does not vary very much if the amount of phosphorus trichloride is increased to 2·2 mols. or reduced to 0·33 mol. The use of phosphorus tribromide gives similar yields. If dioxan–benzene is used as the solvent the yields are lower.

* Since this paper was written Bailey (*J.*, 1950, 3461) has synthesised (I; R = Me) by an alternative method and cyclised it with thionyl chloride–pyridine. He formulates his product as (IV), presumably assuming that direct elimination of methyl chloride has occurred from the intermediate acid chloride as is known to occur in the synthesis of anhydro-*N*-carboxyglycine. It has now been found, however, that his product, m. p. 108°, is identical (mixed m. p.) with our product.

(*b*) 2-Ethoxythiazol-5-one (5 g.) was dissolved in benzene (15 c.c.), and phosphorus tribromide (3 c.c.) added. Addition of water (0·6 c.c.) caused immediate precipitation of an oil which rapidly crystallised. It (2·9 g.) formed long laths, m. p. 110°, from water and was identical (mixed m. p.) with the product obtained as in (*a*).

[2-(3-*Ethylbenzoxazole*)][4-(*thiazolid*-2 : 5-*dione*)]*dimethin*merocyanine (V).—2-2′-Acetanilidovinylbenzoxazole ethiodide (2·2 g.) was dissolved in ethanol (150 c.c.), the solution was cooled to 30°, and triethylamine (0·5 c.c.) and the dione (0·6 g.) were added. After 2 hours the *dye* which had separated was collected, boiled out with ethanol, and obtained as orange leaflets, m. p. 248°, from pyridine–benzene (Found : N, 9·65. $C_{14}H_{13}O_3N_3S$ requires N, 9·7%). If the above components were refluxed in ethanol (10 c.c.) for 15 minutes the yellow solution became deep crimson, and a dye separated. It imparted a pink colour to water and was insoluble in benzene. It gave a magenta solution in cold alcohols or nitrobenzene (red when hot), and a yellow solution in acetone. It formed sepia leaflets, m. p. 257°, from nitrobenzene (Found : C, 58·0; H, 5·0; N, 8·35; S, 8·9. $C_{14}H_{13}O_4N_3S$ requires C, 57·5; H, 5·4; N, 8·4; S, 9·6%). It is a weak photographic sensitizer.

Polyglycylglycine.—The dione (1 g.) was dissolved in water (15 c.c.) and heated on the steam-bath. The polymer separated after 1 minute. The white amorphous solid was repeatedly boiled out with water. It darkened slightly at about 300° (Found : N, 21·5; S, 0·65%).

N-*Thioncarbethoxy*-DL-*alanine* (VII).—Ethyl ethoxydithioformate (35 g.) in alcohol (40 c.c.) was added to a solution of DL-alanine (20·8 g.) and potassium hydroxide (12·1 g.) in water (40 c.c.) and refluxed on the steam-bath for 24 hours. The solution was concentrated to half volume and acidified with concentrated hydrochloric acid. The solid *ester* (21 g.) formed white prisms, m. p. 103·5°, from water (Found : S, 17·8. $C_6H_{11}O_2NS$ requires S, 18·1%).

N-*Thioncarbethoxysarcosine* (VI).—Ethyl ethoxydithioformate (8·5 g.) in alcohol (10 c.c.) was added to a solution of sarcosine (5·0 g.) and potassium hydroxide (3·2 g.) in water (10 c.c.), and the whole refluxed on the steam-bath for 24 hours. After concentration to half volume the clear solution was acidified with concentrated hydrochloric acid and after chilling in ice the solid *product* (9·5 g.) was obtained as a colourless powder, m. p. 86°, from aqueous ethanol (Found : S, 18·3. $C_6H_{11}O_2NS$ requires S, 18·1%).

RESEARCH LABORATORIES, KODAK LTD., HARROW, MDDX.
VEI 2961, SMESTAD, OSLO, NORWAY.

[*Received, March 15th*, 1951.]

---

478. *The Separation of Acids by Paper Partition Chromatography.*

By A. G. LONG, J. R. QUAYLE, and R. J. STEDMAN.

The use of various basic solvent systems for the paper partition chromatography of certain organic acids has been investigated, and a method has been evolved for their separation.

The study has been extended to include anions of amino-acids and of inorganic, partly esterified phosphoric and sulphonic acids, as well as phenols and metallic cations. The application of the method to oxidative degradation studies has been indicated.

DURING structural studies on complex naturally occurring substances it is frequently necessary to work with very small quantities of material; oxidative degradations involve the separation and identification of acidic compounds on such a small scale. The technique of paper partition chromatography is peculiarly suited to the separation of substances on a micro-scale, and its application to acids has now been investigated with a view to evolving a method suitable for general use.

The dimerisation and ionic dissociation of many organic acids render their partition between solvents dependent on concentration, and complicate any separation based on distribution. Furthermore, the volatility of lower fatty acids and phenols precludes the possibility of any chromatography of the unmodified compounds on paper sheets. The various methods hitherto tried with a view to overcoming these difficulties (for reviews, see Elsden, *Biochem. Soc. Symposia*, 1949, No. 3, p. 74; Martin, *Ann. Reports*, 1948, **45**, 282; *Ann. Rev. Biochem.*, 1950, **19**, 531) can be classified under two headings : (*a*) methods involving prior modification of the acidic function, *e.g.*, by esterification (Boldingh, *Rec. Trav. chim.*, 1950, **69**, 247) or by formation of the derived hydroxamates (Fink and Fink, *Proc. Soc. Exp. Biol.*, N.Y., 1949, **70**, 654); and (*b*) methods depending on the control of pH by the presence of excess of volatile acids (Lugg and Overell, *Nature*, 1947, **160**, 87; cf. Synge, *Biochem. Soc. Symposia*, 1949, No. 3, p. 90) or bases (Brown and Hall, *Nature*, 1950, **166**, 66; Hiscox and Berridge, *ibid.*, p. 522; Brown, *Biochem. J.*, 1950

47, 598; *Nature*, 1951, **167**, 441). Of these alternatives, methods of the second type, entailing the simplest operating conditions, were preferred for the present work. The choice of basic in preference to acidic solvent systems was governed by the more effective variations possible in their composition, and by the fact that volatile acidic compounds are not lost during the separation. Hence, in all experiments the solvent was a solution of a base in an aqueous alcohol, usually a single-phase system.

By observing standard experimental procedure it is possible to obtain a series of reproducible R_F values. On Whatman No. 54 paper with ethanolic ammonia as the solvent, the various types of acids separate into the following broad zones, defined by their R_F values: aliphatic polycarboxylic acids and aromatic carboxylic acids containing three or more carboxyl groups, 0—0·25; aliphatic dicarboxylic acids, 0·3—0·6; aromatic dicarboxylic acids, 0·4—0·5; aliphatic monocarboxylic acids, 0·7—0·8. Furthermore, inorganic, sulphonic, and partly esterified phosphoric acids, amino-acids, and certain phenols may be separated in this manner. The R_F values obtained for the homologous series of aliphatic mono- and di-carboxylic acids were used to calculate the corresponding series of R_M values (Bate-Smith and Westall, *Biochim. Biophys. Acta*, 1950, **4**, 427). An approximately linear relationship was found to exist between this value and the number of methylene groups in the acids (Figs. 1 and 2).

The R_F value of a particular ion depends on three independently variable factors, namely, texture of paper and nature of base and of alcohol. Whatman No. 54 paper gives lower R_F

FIG. 1.

Monocarboxylic acids, $H\cdot[CH_2]_n\cdot CO_2H$.

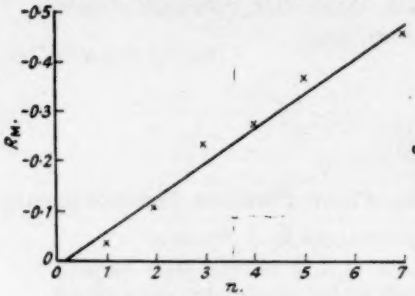
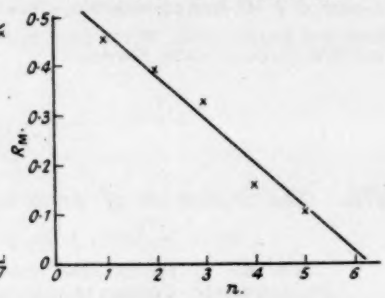


FIG. 2.

Dicarboxylic acids, $[CH_2]_n(CO_2H)_2$.



values than No. 1; previous washing of the paper has no effect on the chromatogram beyond accelerating the movement of the solvent. The organic bases investigated give higher R_F values than does ammonia; *e.g.*, oxalic acid moved at R_F 0·31 in ethanolic ethylamine, whereas in ethanolic ammonia it exhibited a characteristic streak from the starting line. The use of higher alcohols than ethanol reduced the R_F values. Considerable adjustment can be effected by attention to these various factors; for instance, the R_F value of the acetate ion can be increased from 0·28, when *tert.*-butanol–ammonia is used, to 0·81 with ethanol–morpholine. The presence of a metal cation causes no variation in the R_F value of the associated anion, and its presence does not affect the detection of the anion, except in a few cases where the ions separate incompletely. Under standard conditions the R_F value of a given anion is accurately reproducible, a fact attributable perhaps to the ready equilibration of the volatile solvent system.

For the detection of the acidic compounds, B.D.H. Universal Indicator is very satisfactory and was preferred to the indicators recommended by Brown and Hall, and by Hiscox and Berridge (*locc. cit.*). The spots fade in air, but the colours may be restored by further spraying.

Ninhydrin has been used extensively to detect amino-acids, the development of the colour being due to initial reduction of the ninhydrin to hydrindantin by the amino-acid, followed by the formation of the intensely coloured diketoindanylideneaminoindanedione (Ruhemann, *J.*, 1911, **99**, 792, 1486; Moore and Stein, *J. Biol. Chem.*, 1948, **176**, 367). This reaction proceeds to some extent with amides or ammonium salts, and hence its applicability to the detection of the acid salts on paper was investigated. In many cases its sensitivity was found to be greater than that obtained by spraying with indicator, and the resulting spots were permanent. The method is not as sensitive for the ammonium salts as it is for amino-acids, a fact attributable to the lack of hydrindantin in the former case, and therefore some source of this compound was

sought. Ene-diols cause the desired reduction of ninhydrin to hydrindantin (West and Rinehart, *ibid.*, 1942, **146**, 105), and in fact, the inclusion of ascorbic acid in the reagent solution increases its sensitivity (cf. Tetzner, *Mikrochem.*, 1940, **28**, 141). However, the background colour, probably due to traces of the base strongly associated with the paper, is likewise more intense; this modification therefore does not greatly faciliate the detection of ammonium salts on paper, and has not been studied further (cf. Fowden, *Biochem. J.*, 1951, **48**, 327).

The oxidation of iodide by iodate depends on the presence of hydrogen ions, and this furnishes a further method for the detection of regions of acidity on the paper (cf. Buchanan, Dekker, and Long, *J.*, 1950, 3162). In the present instance, the free acids may be generated by thermal decomposition of their ammonium salts, and iodine is then liberated at the sites of the various fractions when a mixture of sodium iodate and sodium iodide is applied as a spray; starch increases the sensitivity. The method was originally used successfully for the detection of acylamido-acids (G. W. Kenner, private communication), but is unreliable for the simpler acids. This may be due to the volatility of the acids themselves, or to the predominance of amide formation (cf. Degering, "An Outline of Organic Nitrogen Compounds," University Lithoprinters, Michigan, 1945, p. 400).

Several other methods of detection were tried with limited success (see Experimental section). The sensitivity of the various methods varies from compound to compound: 20—100 μg. of material is a safe working range, although particular compounds can be detected at concentrations considerably below this. Fractions may be differentiated from each other not only on the basis of R_F values, but also, in some cases, by the application of specific spraying reagents (see Experimental section).

The applicability of the method to the separation of products from micro-oxidations was tested with the following compounds, alkaline permanganate or hydrogen peroxide being used as oxidising agents: formaldehyde to formic acid; benzaldehyde to benzoic acid; propane-1 : 2-diol to acetic and formic acids; benzyl alcohol to benzoic acid. The oxidation products were identified by the methods described above. On a larger scale a mixture (100 mg.) of benzoic and malonic acids was quantitatively separated on a column of powdered cellulose, ethanolic ammonia being used as the developing solvent.

The method has been applied to structural studies, and further examples of its use will be found in subsequent communications on several natural products.

Experimental.

The method of paper partition chromatography employing a descending solvent system as described by Consden, Gordon, and Martin (*Biochem. J.*, 1944, **38**, 224) was used. The solvent front was allowed to move a distance of about 30 cm., which, in the case of ethanolic solvents, took approximately 8 hours on Whatman No. 1 paper at 19—20°. The inclusion of *n*-butanol in the solvent mixture retarded the progress of the solvent front, and with *tert.*-butanol it was necessary to extend the time of irrigation to 36 hours. The solvents percolated through No. 54 paper more rapidly than through No. 1 paper. Commercial 95% ethanol, 70% ethylamine, and ammonia solution (AnalaR; *d* 0·88) were used throughout. The other bases and alcohols employed were distilled before use. Whatman No. 1 and No. 54 papers only were employed, and, for experiments with washed paper, the sheets were treated successively with 2N-acetic acid (A.R.; 6 times), distilled water (3 times), 2N-ammonia solution (A.R.; 6 times), and finally with distilled water until neutral. They were dried at 100°.

The chromatograms were run with 20—100 μg. of material, applied in the form of a 0·2—1·0% aqueous solution of the free acid or its ammonium or alkali-metal salt.

Location of Spots.—(a) *Ninhydrin method.* The papers were dried at 80° for 15 minutes and sprayed with a 0·2% solution of ninhydrin in ethanol containing formic acid (5% v/v), then heated for a few minutes at 100—120°. The ammonium salts appeared as bluish spots on a paler background of bluish-pink. No. 1 paper was found to be more suitable when ninhydrin was used, as poor contrast between the spots and the background was obtained with No. 54 paper. The sensitivity of the method varied; *e.g.*, the spot from 20 μg. of acetic acid was of equal intensity to that given by 100 μg. of benzoic acid. The utility of this method of locating spots was limited to chromatography using ammonia solution as the base. In the case of ethylamine systems, a strong background colour was given even by papers which had been heated for 2 hours at 120° before being sprayed with ninhydrin solution. The sensitised ninhydrin reagent was prepared by dissolving ninhydrin (200 mg.) and ascorbic acid (50 mg.) in 95% ethanol (100 c.c.); it was used either in this state or mixed with formic acid (5 c.c.).

(b) *Indicator method.* The papers were dried at 80° for 15 minutes and sprayed with B.D.H. Universal Indicator, the pH of which was previously adjusted to 9—10 with sodium hydroxide solution. When ammonia solution was used in the running solvent, the zones appeared immediately and slowly faded, whereas with an organic base the paper turned a uniform greenish colour; on exposure to air the spots gradually appeared. The appearance of acidic bands was observed with some papers. Cations appeared as blue spots.

(c) *Iodate–iodide method.* The papers were heated at 130° for 30 minutes and sprayed with a mixture (1 : 1) of aqueous sodium iodate (0·2%) and iodide–starch (0·4% and 0·5%, respectively). Blue spots appeared within 10 minutes. This method, which gave good results with acylamido-acids, benzoic, oxalic, and toluenesulphonic acids, failed with formic, acetic, cinnamic, and salicylic acids. It was necessary to use No. 1 papers owing to the background colour given by No. 54 papers.

(d) *Miscellaneous methods.* The following reagents were investigated for the detection of ammonium salts, but were found inferior to the above: Nessler's reagent (cf. Libermann, Zaffaroni, and Stotz, *J. Amer. Chem. Soc.*, 1951, **73**, 1387), and phenol and sodium hypochlorite solution (Snell and Snell, "Colorimetric Methods of Analysis," van Nostrand, New York, 1937, p. 345). Unsuccessful attempts were made to convert the acids on the paper into benziminazoles (Hickinbottom, "Reactions of Organic Compounds," Longmans, Green and Co., London, 1948, p. 326), which would be detectable in ultra-violet light (cf. Buchanan, Johnson, Mills, and Todd, *J.*, 1950, 2845), and to detect them by decomposition of their silver salts in ultra-violet light.

(e) *Methods for specific compounds.* Additional information concerning the nature of some of the fractions was obtained by the use of the following selective spraying reagents: ammoniacal silver nitrate for differentiating between formic and acetic acids; a solution (2%) of iodine in ethanol for phenols and certain acids (cf. Brante, *Nature*, 1949, **163**, 651; Marini-Bettolo-Marconi and Guarino, *Experientia*, 1950, **6**, 309); alkaline permanganate solution for unsaturated acids (Pacsu, Mora, and Kent, *Science*, 1949, **110**, 446); diazonium salt solutions (Bray, Thorpe, and White, *Biochem. J.*, 1950, **46**, 271) and ammonium phosphomolybdate (Riley, *J. Amer. Chem. Soc.*, 1950, **72**, 5782) for phenols. Simple inspection of the paper under ultra-violet light revealed fluorescent (or dark) spots in the case of such aromatic compounds as salicylic acid and α- and β-naphthols.

Limits of Resolution.—It is generally possible to resolve a mixture of two substances having R_F values differing by not less than 0·05 (*i.e.*, a separation of 1·5 cm. in a normal chromatogram).

Characteristics of Individual Acids.—The R_F values obtained for a variety of acids on Whatman No. 54 paper when ethanol (80), ammonia solution (4; *d* 0·88), and water (16) were used as the solvent system are listed in Table I. B.D.H. Universal Indicator was used for detection, unless otherwise stated.

TABLE I.

Aliphatic monocarboxylic acids. Formic (0·50), acetic (0·52), propionic (0·56), butyric (0·64), valeric (0·65), hexanoic (0·70), octanoic (0·74), *iso*butyric (0·64), *iso*valeric (0·67), phenylacetic acid (0·60).

Aliphatic halogeno-acids. Trifluoroacetic (0·75), chloroacetic (0·52), dichloroacetic (0·60), trichloroacetic (0·70), bromoacetic (0·54), β-chloropropionic (0·60).

Aliphatic hydroxy-acids. Citric (0·11), lactic (0·49), malic (0·25), tartaric (0·19).

Aliphatic and other amino-acids.[1] Alanine (0·43), arginine (0·20), aspartic acid (0·18), cystine (0·10), glutamic acid (0·22), glycine (0·26), lysine (0·60), phenylalanine (0·68), proline (0·44), serine (0·32), threonine (0·40), tyrosine (0·48), valine (0·61), carbobenzyloxyphenylalanine (0·83), carbobenzyloxyphenylalanylglycine (0·83).

Aromatic monocarboxylic acids. Benzoic (0·58), *o*-bromobenzoic (0·76), *p*-bromobenzoic (0·76), *m*-chlorobenzoic (0·65), cinnamic (0·68), 2 : 4-dinitrobenzoic (0·60), 3 : 5-dinitrobenzoic (0·60), α-naphthoic (0·69), β-naphthoic (0·69), *m*-nitrocinnamic (0·83), protocatechuic (0·39), salicylic (0·73), *o*-toluic (0·66), *m*-toluic (0·63), *p*-toluic (0·63).

Dicarboxylic acids. Oxalic (0—0·15),[2] malonic (0·26), succinic (0·29), glutaric (0·32), adipic (0·41), pimelic (0·44), maleic (0·31), phthalic (0·39), *iso*phthalic (0·45), terephthalic (0·45).

Other acids. Aconitic (0·16), trimesic (0·00).

Phosphoric acids. Adenosine-5′ benzyl hydrogen phosphate (0·48), adenosine-5′ phosphate (muscle adenylic acid) (0·03).

Sulphonic acids. Sulphanilic (0·53), 1-hydroxynaphthalene-5-sulphonic (0·67), 2-hydroxynaphthalene-6-sulphonic (0·58), toluene-*p*-sulphonic (0·73).

Phenols. Catechol (0·76), 2 : 4-dinitrophenol (0·76), *m*-hydroxybenzaldehyde (0·85), *p*-hydroxybenzaldehyde (0·69), α-naphthol (0·84), β-naphthol (0·82), *m*-nitrophenol (0·83), *p*-nitrophenol (0·66), phloroglucinol (0·61), picric acid (0·71), resorcinol (0·77).

Salts[3] (the italicized figures are values for cations). Sodium salts: fluoride (*0—0·13*, 0·27), chloride (*0·26*, 0·43), bromide (*0·25*, 0·48), iodide (*0·24*, 0·53), acetate (*0·26*, 0·52), azide (*0·26*, 0·54), chromate (0·09), nitrate (*0·28*, 0·48), nitrite (*0·27*, 0·47), phosphate (*0·21*, 0·02), sulphate (*0·20*, 0·09), sulphite (*0·20*, 0·04). Lithium salts: chloride (0·48), nitrate (0·55), phosphate (0·02), sulphate (*0·38*, 0·11). Potassium acetate (*0·19*, 0·52); cæsium alum (*0·10*); magnesium acetate (*0·00*, 0·52); calcium acetate (*0·00*, 0·52).

[1] Amino-acids were run on Whatman No. 1 paper; ninhydrin was used for detection. [2] Oxalic acid forms a characteristic streak in this solvent. More satisfactory results can be obtained in other solvent systems (see below). [3] Cf. Pollard, McOmie, and Elbeih, *J.*, 1951, 470.

The R_F values of some acids under various conditions are listed in Table II. Unless otherwise stated, Whatman No. 1 paper was used.

TABLE II.

Anion.	Solvent system (see below). A.†	B.†	C.	D.	E.	F.	G.	H.†	J.	K.†	L.†
Acetic	0·69	0·81	0·66	0·28	0·44	—	—	0·53	0·67	0·64	0·52
Benzoic	—	—	0·74	0·51	0·67	0·64	0·80	—	0·72	—	0·58
Citric	—	—	0·07	—	—	0·00	*	—	—	—	0·11
Formic	0·70	0·80	0·65	0·33	0·44	—	—	0·53	0·67	0·64	0·50
Oxalic	—	0·53	*	—	—	—	*	0·18	0·35	0·31	*
Phthalic	0·68	0·70	0·38	—	—	0·15	0·67	0·37	0·57	0·52	0·39
Resorcinol	0·77	—	—	—	—	—	—	0·70	—	—	0·77
Salicylic	—	—	—	—	—	0·73	0·69	—	—	—	0·73
Succinic	0·56	0·64	0·42	—	—	0·00	0·64	0·28	0·50	0·42	0·29
Sulphanilic	0·78	—	0·57	—	—	0·18	—	0·61	0·65	0·64	0·53
Tartaric	0·85	—	0·22	—	—	—	*	0·17	0·36	0·29	0·19
Toluene-*p*-sulphonic	0·80	0·73	0·70	—	—	—	0·67	—	—	—	0·73

* These acids give streaks on the paper. † Whatman No. 54 paper.

Solvent systems : (A) Ethanol (32), water (8), *cyclo*hexylamine (3·3); (B) ethanol (32), water (8), morpholine (2·6); (C) ethanol (80), water (16), ammonia (4; *d* 0·88); (D) *tert.*-butanol (80), water (16), ammonia (*d* 0·88) (4); (E) *n*-butanol (40), ethanol (40), water (16), ammonia (4; *d* 0·88); (F) *n*-butanol saturated with 0·75N-aqueous ethylamine; (G) ethanol (80), pyridine (12), water (8); (H) ethanol (80), 33% aqueous ethylamine (20); (J) ethanol (80); 16% aqueous ethylamine (20); (K) as (J); (L) as (C).

Identification of Acids produced in Oxidation Experiments.—Unless otherwise stated, each compound (see Table below) was allowed to react in aqueous solution (1 c.c.; 1%) with the oxidising agent. The resulting solution, clarified if necessary by being centrifuged, was applied to a Whatman No. 1 paper strip in such a way that each drop spread to no more than 0·7 cm. diameter. Satisfactory results were obtained if this was done 3 times, the paper being dried after each addition. The chromatograms were developed with ethanolic ammonia (see Table I), and the fractions located with ninhydrin. In each case behaviour corresponding with that of the expected acidic products, which were run alongside, was observed.

Substance.	Oxidising agent.	Reaction time.	R_F Values of products.
Formaldehyde	$KMnO_4$ (1 c.c.) [1]	4 hrs.	0·60 (formic acid)
Benzaldehyde	$KMnO_4$ (1 c.c.)	4 hrs.	0·63 (acetic acid) [2] 0·73 (benzoic acid)
Propane-1 : 2-diol	$KMnO_4$ (1 c.c.)	3 hrs.	0·65 (formic + acetic acids) [3]
Benzyl alcohol [4]	$KMnO_4$ (2 c.c.)	12 hrs.	0·58 (benzoic acid) [5]
Formaldehyde	H_2O_2 (1 c.c.; 20-vol.), Na_2CO_3 (0·5 c.c.; 3N.)	4 hrs.	0·60 (formic acid)
Benzaldehyde	do.	4 hrs.	0·63 (acetic acid) [2] 0·73 (benzoic acid)
Propane-1 : 2-diol	H_2O_2 (0·5 c.c.; 100-vol.), aq. NH_3 (0·5 c.c.; *d* 0·88); 100°	5 mins.[6]	0·65 (formic + acetic acids) [3]

[1] The alkaline permanganate solution was prepared as described by Pacsu, Mora, and Kent (*loc. cit.*). [2] Oxidation was carried out in aqueous-ethanolic solution, which was shown by blank experiments to yield some acetic acid under these conditions. [3] It was impossible to distinguish by their R_F values these two acids, both of which would be expected as oxidation products. [4] A 0·3% aqueous solution was used. [5] Whatman No. 54 paper. [6] The reagents were evaporated under reduced pressure, and the oxidation repeated. Finally, the products were dissolved for chromatography in 0·5N-ammonia solution (1 c.c.).

Separation of Benzoic and Malonic Acids on a Cellulose Column.—Cellulose (34 g.), prepared by shredding Whatman "Ashless" tablets through an 80-mesh sieve, was packed into a column (16 × 4 cm.) and a solution of 8-hydroxyquinoline (200 mg.) was washed through with the usual ethanol–ammonia solvent in order to remove metallic cations. Further solvent (300 c.c.) was run through after complete elution of the hydroxyquinoline. A mixture of benzoic (50 mg.) and malonic acids (50 mg.) was put on the column, and fractions (5 c.c.) of the eluate were collected. The samples were tested by spotting on to a filter-paper and developing this with ninhydrin as previously described. The benzoic acid was eluted in fractions 16—19, and the malonic in fractions 39—44; the acids were recovered quantitatively from these fractions.

The authors thank Professor A. R. Todd, F.R.S., and Drs. A. W. Johnson and G. W. Kenner for their interest and advice. The above work was carried out during the tenure of a Scholarship from Glaxo Laboratories, Ltd. (A. G. L.), a University of Wales Fellowship (J. R. Q.), and a Maintenance Allowance from the Department of Scientific and Industrial Research (R. J. S.).

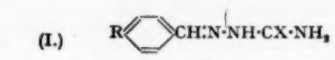
UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, April 21st,* 1951.]

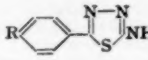
479. *Compounds related to Thiosemicarbazide. Part VIII.* The Oxidation of Thiosemicarbazones.†*

By Eric Hoggarth.

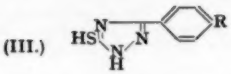
The oxidation of benzaldehyde thiosemicarbazone with hydrogen peroxide in cold acetic acid gives some novel compounds, investigation of which has shown that they are probably derivatives of 2 : 3-diazabuta-1 : 3-diene.

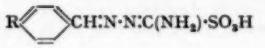
The oxidation of benzaldehyde thiosemicarbazone (I; R = H, X = S) was first investigated by Young and Eyre (*J.*, 1901, **79**, 54), who found that with aqueous ferric chloride solution, loss of two hydrogen atoms took place very readily to give 2-amino-5-phenyl-1 : 3 : 4-thiadiazole (II; R = H). The formation of a very small amount of an insoluble, high-melting substance was thought to indicate the simultaneous formation of the isomeric 3-phenyl-1 : 2 : 4-triazole-5-thiol (III; R = H). The formation of aminothiadiazoles by oxidation of thiosemicarbazones with ferric chloride has been confirmed by a number of workers including De and Roy Choudhury (*J. Indian Chem. Soc.*, 1928, **5**, 269), who denied that triazoles were also formed. However, these workers claimed that oxidation of thiosemicarbazones with perhydrol in alcohol gave compounds derived from the triazole (III), usually the corresponding disulphide.

(I.) 

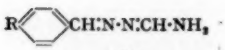


(II.)

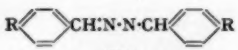
(III.) 



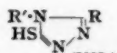
(IV.)



(V.)



(VI.)



(VII.)

Investigation of the oxidation of benzaldehyde thiosemicarbazone showed that perhydrol in cold acetic acid gave two novel oxidation products. One of these was an acid, to which, upon the evidence mentioned below, the constitution 1-amino-4-phenyl-2 : 3-diazabuta-1 : 3-diene-1-sulphonic acid (IV; R = H) was ascribed, and the other an unstable oily base (isolated as its picrate) which was thought to be 1-amino-4-phenyl-2 : 3-diazabuta-1 : 3-diene (V; R = H). Under similar conditions, *p*-methoxybenzaldehyde thiosemicarbazone gave two compounds (IV and V; R = OMe) both of which were crystalline. The basic one, however, was still unstable, and with other thiosemicarbazones examined, only the corresponding sulphonic acids were isolated.

The constitution of the sulphonic acids (IV) followed from the products of their hydrolyses. When heated with concentrated hydrochloric acid, the acids (IV; R = H or OMe) quickly dissolved with almost immediate separation of the corresponding azines (VI; R = H or OMe) and a solution of the same acids in dilute sodium carbonate solution, when boiled, rapidly deposited the corresponding semicarbazones (I; R = H or OMe, X = O). The bases (V; R = H or OMe) were also readily hydrolysed to the azines, and attempts to crystallise (V; R = H) always resulted in formation of benzaldehyde azine. The constitution of the basic compounds was confirmed by their formation from the thiosemicarbazones by " desulphurisation " with Raney nickel catalyst.

Although it is known that in the presence of strong acids thiourea is first oxidised to a salt of " formamidine disulphide " (Preisler and Berger, *J. Amer. Chem. Soc.*, 1947, **69**, 322), yet it was shown by Barnett (*J.*, 1910, **97**, 63) that under approximately neutral conditions hydrogen peroxide gives aminoiminomethanesulphinic acid (" formamidine sulphinic acid ") and that this compound readily loses sulphur dioxide giving (presumably) formamidine. Böeseken (*Rec. Trav. chim.*, 1936, **55**, 1044) showed that aminoiminomethanesulphinic acid could be oxidised by cold peracetic acid to the corresponding sulphonic acid, $NH_2 \cdot C(:NH) \cdot SO_3H$. It

* Part VII, *J.*, 1950, 1582. † Patent protection pending.

seems probable, therefore, that the oxidation of thiosemicarbazones by perhydrol in cold acetic acid gives a mixture of the sulphonic acid (IV) and the corresponding sulphinic acid, the latter losing sulphur dioxide during the isolation procedure. It was found by Kitamura (*J. Pharm. Soc. Japan*, 1937, **57**, 51) that thiosemicarbazide was oxidised by perhydrol in *alkaline* solution, giving semicarbazide, and that a similar reaction took place (more slowly) with thiosemicarbazones. It can be supposed that in Kitamura's experiments the sulphonic acids were first formed and suffered hydrolysis. De and Roy Choudhury's oxidations (*loc. cit.*) were effected with perhydrol in alcohol, the mixture being allowed to become hot as reaction took place. Except for benzaldehyde thiosemicarbazone, the thiosemicarbazones examined by these authors carried substituents upon the 4-nitrogen atom of the thiosemicarbazide residue, and all, with the same exception, gave disulphides of 3 : 4-disubstituted 4 : 1 : 2-triazole-5-thiols (VII). In the case of benzaldehyde thiosemicarbazone the product was claimed to be 3-phenyl-1 : 2 : 4-triazole (thought to arise from a corresponding thiol or disulphide by elimination of the sulphur atom) although the melting point of the compound isolated (177°) was not in agreement with that found by other workers (*e.g.*, Young and Oates, *J.*, 1901, **79**, 659). On oxidising benzaldehyde thiosemicarbazone under De and Roy Choudhury's conditions, we found the principal product to be 1-amino-4-phenyl-2 : 3-diazabuta-1 : 3-diene (V; R = H), identified as its picrate and by hydrolysis to benzaldehyde azine. A small amount of a crystalline substance also isolated (m. p. 164°) proved to be unoxidised thiosemicarbazone. Analogous results were obtained by oxidising *p*-anisaldehyde thiosemicarbazone under the same conditions, the base (V; R = OMe) in this case being obtained crystalline and identified by mixed m. p. determination.

Two thiosemicarbazones having a methyl group in position 4 of the thiosemicarbazide residue were oxidised with perhydrol in cold acetic acid. The corresponding sulphonic acids alone were isolated, though there was a considerable basic fraction which could not be induced to crystallise.

Experimental.

Oxidation of Benzaldehyde Thiosemicarbazone.—(*a*) Perhydrol (100 c.c.) and glacial acetic acid (400 c.c.) were stirred at 0°, and finely powdered benzaldehyde thiosemicarbazone (30·0 g.) added during 0·5—0·75 hour. The thiosemicarbazone at first passed into solution but crystals quickly separated and the mixture became quite thick. Stirring was continued for 4—5 hours at 0° and the temperature was then allowed to rise gradually (overnight) to 15—20°. Water (2 l.) was added, and the precipitate (16·0 g.; m. p. 212—214°) collected, washed with a little water, and dried at 80°. The filtrate was concentrated (at 25—30° in a good vacuum) to 200 c.c. and cooled, and concentrated hydrochloric acid added. The precipitate (4·1 g.; m. p. 208—210°) was collected, washed and dried as before, united with the previous precipitate, and dissolved in water (250 c.c.) by stirring and adding solid potassium hydrogen carbonate until effervescence ceased. The clear, filtered solution was made acid with concentrated hydrochloric acid, and the *1-amino-4-phenyl-2 : 3-diazabuta-1 : 3-diene-1-sulphonic acid* (IV; R = H) (17·4 g.) collected and crystallised from alcohol or acetic acid, giving colourless needles, m. p. 254—256° (Found : C, 42·1; H, 4·1; N, 19·0; S, 13·9. $C_8H_8O_3N_3S$ requires C, 42·3; H, 4·0; N, 18·5; S, 14·1%). The filtrate from the second crop of sulphonic acid was cooled strongly and made alkaline with concentrated sodium hydroxide solution, the precipitated oil extracted with ether, dried, and filtered, and the solvent removed (under reduced pressure without heating), giving a clear yellow oil (3·8 g.) which could not be distilled at 0·02 mm. pressure. Attempts to crystallise it gave benzaldehyde azine as yellow plates, m. p. 92° not depressed by an authentic specimen (Found : N, 13·8. Calc. for $C_{14}H_{12}N_2$: N, 13·4%). On storage, a strongly basic smell became apparent and crystals separated which proved also to be the azine. The freshly isolated oil (1·0 g.) was dissolved in cold alcohol (10 c.c.), and the solution filtered and quickly added to a solution of picric acid (2·0 g.) in alcohol (20 c.c.); crystalline aggregates (1·2 g.), m. p. 210—211°, slowly separated (Found : C, 44·7; H, 3·4; N, 22·6. $C_8H_9N_3.C_6H_3O_7N_3$ requires C, 44·7; H, 3·2; N, 22·4%). This *picrate* could not be recrystallised, and attempts to regenerate the base gave only benzaldehyde azine.

When the above sulphonic acid (2·0 g.) was boiled with concentrated hydrochloric acid (20 c.c.) and acetic acid (10 c.c.), a yellow solid (0·8 g., m. p. 90—92°) separated on cooling and neutralisation with potassium hydrogen carbonate. From alcohol, bright yellow needles of benzaldehyde azine, m. p. and mixed m. p. 93—94°, were obtained (Found : C, 80·6; H, 5·7; N, 14·0. Calc. for $C_{14}H_{12}N_2$: C, 80·8; H, 5·8; N, 13·4%). When the sulphonic acid (2·3 g.) was refluxed for 6 hours with 5% sodium carbonate solution (50 c.c.), a solid (1·3 g.; m. p. 218—220°) separated and after cooling was collected and crystallised from alcohol, giving long faintly coloured needles of benzaldehyde semicarbazone, m. p. and mixed m. p. 224—226° (Found : C, 59·2; H, 5·7; N, 26·2. Calc. for $C_8H_9ON_3$: C, 58·9; H, 5·5; N, 25·8%). A solution of 1-amino-4-phenyl-2 : 3-diazabuta-1 : 3-diene in N-hydrochloric acid became cloudy when heated, and, by ether extraction, benzaldehyde azine was isolated; it crystallised from alcohol, giving yellow needles, m. p. and mixed m. p. 92—93°.

(*b*) Finely powdered benzaldehyde thiosemicarbazone (3·6 g.) was added to a well stirred mixture of perhydrol (5 c.c.) and alcohol (50 c.c.) without external cooling, solution taking place with rise of temperature (70—75°). After 0·5 hour's stirring, a small amount of colloidal sulphur was removed (charcoal) and the clear pale yellow filtrate was evaporated at 25° in a good vacuum. The sticky

residue was shaken twice with N-hydrochloric acid (50 c.c.) and ether (50 c.c.), the united extracts filtered from a small insoluble residue, and the ethereal layer separated. The solvent was removed from the ethereal extract and the small residue crystallised twice from aqueous alcohol, giving colourless needles (0·1 g.) of benzaldehyde thiosemicarbazone, m. p. and mixed m. p. 163°. The acid extract was cooled strongly, made alkaline with 10N-sodium hydroxide, and extracted with ether; the extracts were dried and evaporated without being heated, giving a pale yellow oil (1·5 g.). The picrate prepared as above formed yellow aggregates, m. p. 210—212° not depressed by the compound obtained as in (*a*) (Found: C, 44·6; H, 3·1%). The oil (1·2 g.) was refluxed with concentrated hydrochloric acid (10 c.c.) for 5 minutes, cooled, and extracted with ether, and the oil left on evaporation of the solvent crystallised from aqueous alcohol, giving yellow needles (0·65 g.) of benzaldehyde azine, m. p. and mixed m. p. 93—94°.

Oxidation of p-*Anisaldehyde Thiosemicarbazone.*—(*a*) *p*-Anisaldehyde thiosemicarbazone (33·4 g.) being used in place of the benzaldehyde compound in (*a*) above, two crops of a crude acid (27·2 g., m. p. 250—252°; and 1·1 g., m. p. 245—250°) were obtained which were united and purified by solution in dilute potassium hydrogen carbonate solution, giving 1-*amino*-4-p-*methoxyphenyl*-2 : 3-*diazabuta*-1 : 3-*diene*-1-*sulphonic acid* (IV; R = OMe), which crystallised from acetic acid in colourless prisms (18·2 g.), m. p. 256—257° (Found: C, 42·2; H, 4·5; N, 16·4; S, 12·0. $C_9H_{11}O_4N_3S$ requires C, 42·0; H, 4·3; N, 16·3; S, 12·5%). The acid filtrate from the second crop of sulphonic acid was cooled strongly and made alkaline with 10N-sodium hydroxide; the resulting oil was allowed to harden, collected, washed with water, and dried (P_2O_5), and the 1-*amino*-4-p-*methoxyphenyl*-2 : 3-*diazabuta*-1 : 3-*diene* (V; R = OMe) (1·2 g.; m. p. 100—102°) crystallised from benzene–light petroleum (b. p. 60—80°), giving long colourless glistening needles or plates (0·65 g.), m. p. 112—113° (Found: C, 61·3; H, 6·2; N, 24·2. $C_9H_{11}ON_3$ requires C, 61·1; H, 6·2; N, 23·8%). The *picrate*, which slowly separated when warm, filtered, alcoholic solutions of base and picric acid were mixed, formed long yellow needles, m. p. 198—200°, which could not be recrystallised (Found: C, 44·2; H, 3·7; N, 21·0. $C_9H_{11}ON_3.C_6H_3O_7N_3$ requires C, 44·3; H, 3·5; N, 20·7%). Hydrolysis of the sulphonic acid (2·5 g.) with concentrated hydrochloric acid and with 10% sodium carbonate solution as described for the phenyl compound gave respectively, *p*-anisaldehyde azine, which crystallised from xylene in colourless clumps of prisms (1·0 g.), m. p. and mixed m. p. 170° (Found: C, 72·0; H, 6·0. Calc. for $C_{16}H_{16}O_2N_2$: C, 71·7; H, 6·0%), and *p*-methoxybenzaldehyde semicarbazone, which crystallised from alcohol in nearly colourless leaflets (0·7 g.), m. p. and mixed m. p. 211° (Found: N, 22·4. Calc. for $C_9H_{11}O_2N_3$: N, 21·8%). 1-Amino-4-*p*-methoxyphenyl-2 : 3-diazabuta-1 : 3-diene (1·0 g.), heated for a few minutes with concentrated hydrochloric acid, gave *p*-anisaldehyde azine (0·5 g.), m. p. and mixed m. p. 170°.

(*b*) Oxidation of *p*-anisaldehyde thiosemicarbazone (4·2 g.) in place of the benzaldehyde compound in (*b*) above gave unoxidised thiosemicarbazone (0·5 g.), m. p. and mixed m. p. 170—171°, and 1-amino-4-*p*-methoxyphenyl-2 : 3-diazabuta-1 : 3-diene (0·7 g.), m. p. 112—113° (Found: C, 60·9; H, 6·2%). The picrate, formed as previously, gave yellow needles, m. p. 196—198° (Found: C, 44·6; H, 3·5%). There was a considerable resinous residue insoluble in both N-hydrochloric acid and ether from which nothing but a small amount of unoxidised thiosemicarbazone was isolated.

1-*Amino*-4-*phenyl*-2 : 3-*diazabuta*-1 : 3-*diene* (V; R = H).—Benzaldehyde thiosemicarbazone (4·5 g.), alcohol (125 c.c.), and Raney nickel catalyst (*ca.* 20·0 g.) were refluxed for 3 hours with stirring, filtered, and evaporated at 35—40° under reduced pressure. The residual oil (3·2 g.) was dissolved in ether and filtered, and the solvent removed under reduced pressure. The picrate, formed as above, separated as yellow aggregates, m. p. 209—211° (Found: C, 45·3; H, 3·1%). The diene (1·0 g.) was refluxed with concentrated hydrochloric acid (10 c.c.) for 1 hour and cooled, the oil extracted with ether, dried, and evaporated, and the residue crystallised from dilute alcohol, giving benzaldehyde azine, which formed yellow needles (0·5 g.), m. p. and mixed m. p. 93° (Found: C, 80·8; H, 5·9%).

1-*Amino*-4-p-*methoxyphenyl*-2 : 3-*diazabuta*-1 : 3-*diene* (V; R = OMe).—On use of *p*-methoxybenzaldehyde thiosemicarbazone (5·2 g.) in the above experiment, the crystalline residue left on removal of the alcohol at 35—40° crystallised from benzene–light petroleum (b. p. 60—80°) in colourless plates (3·0 g.), m. p. 110—111° (Found: C, 60·8; H, 6·2; N, 24·2%). The picrate, formed as previously, separated as yellow needles, m. p. 198—200° (Found: C, 44·3; H, 3·7%).

The following sulphonic acids were obtained by oxidation of the corresponding thiosemicarbazones with perhydrol in cold acetic acid: 1-*Amino*-4-p-*ethylsulphonylphenyl*-2 : 3-*diazabuta*-1 : 3-*diene*-1-*sulphonic acid hydrate* (IV; R = SO_2Et), small colourless needles (from acetic acid), m. p. 242° (Found: C, 35·8, 35·9; H, 4·5, 4·3; S, 19·1. $C_{10}H_{12}O_5N_2S,H_2O$ requires C, 35·6; H, 4·5; S, 19·0%), which on being dried at 120° in a vacuum gave the anhydrous *acid*, m. p. 242—244° (Found: C, 37·0; H, 4·5. $C_{10}H_{12}O_5N_2S$ requires C, 37·6; H, 4·1%). 1-*Amino*-3-p-*acetamidophenyl*-2 : 3-*diazabuta*-1 : 3-*diene*-1-*sulphonic acid* (IV; R = NHAc), which was insoluble in all ordinary solvents and was purified by solution in cold dilute potassium hydrogen carbonate solution and precipitation with acetic acid, giving micro-needles, m. p. 199—201° (decomp.) (Found: C, 41·7; H, 5·0; S, 11·3. $C_{10}H_{12}O_4N_4S$ requires C, 42·3; H, 4·2; S, 11·3). 1-*Methylamino*-4-*phenyl*-2 : 3-*diazabuta*-1 : 3-*diene*-1-*sulphonic acid*, colourless flat needles, m. p. 232—234° (decomp.) (Found: C, 44·8; H, 4·6. $C_9H_{11}O_3N_3S$ requires C, 44·8; H, 4·5%). 4-p-*Methoxyphenyl*-1-*methylamino*-2 : 3-*diazabuta*-1 : 3-*diene*-1-*sulphonic acid*, colourless leaflets or plates, m. p. 216—218° (slight decomp.) (Found: C, 43·9; H, 5·1; S, 11·6. $C_{10}H_{13}O_4N_3S$ requires C, 44·3; H, 4·8; S, 11·8%).

IMPERIAL CHEMICAL INDUSTRIES LIMITED,
RESEARCH LABORATORIES, BLACKLEY, MANCHESTER, 9.

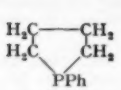
[*Received, April 27th*, 1951.]

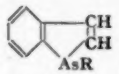
480. *The Synthesis of* 1-*Substituted Phosphindolines.*

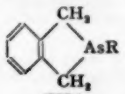
By Frederick G. Mann and Ian T. Millar.

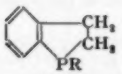
Synthesis of 1-ethylphosphindoline is described by a method that should be applicable to many 1-alkyl(or aryl)-phosphindolines.

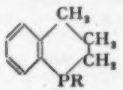
Hitherto the only recorded compound containing a five-membered ring system consisting solely of carbon and phosphorus atoms has been 1-phenyltetramethylenephosphine (I) (Grüttner and Krause, *Ber.*, 1916, **49**, 438). In contrast, a much greater variety of compounds containing a five-membered carbon–arsenic ring system is known : for example, the arsenic analogue of (I)


(I.)


(II.)

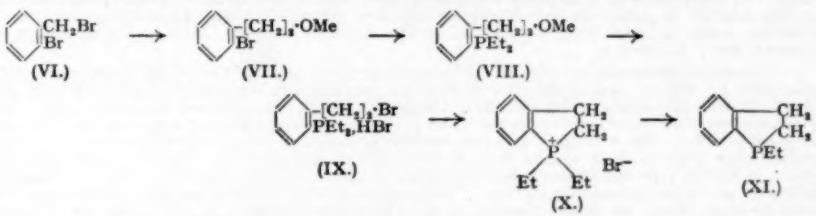

(III.)


(IV.)


(V.)

(Grüttner and Krause, *loc. cit.*), the 1-substituted arsindoles (II) (Das Gupta, *J. Indian Chem. Soc.*, 1937, **14**, 231, 349, 397, 400) and the corresponding arsindolines (Turner and Bury, *J.*, 1923, **123**, 2489), and the *iso*arsindolines (III) (Lyon and Mann, *J.*, 1945, 30; Lyon, Mann, and Cookson, *J.*, 1947, 662; Beeby, Cookson, and Mann, *J.*, 1950, 1917). We have now developed a synthesis of 1-alkylphosphindolines (IV) which is closely parallel to that already employed for 1-alkyltetrahydrophosphinolines (V) by Beeby and Mann (*J.*, 1951, 411).

For this purpose, *o*-bromobenzyl bromide (VI) was converted as before by the action of one atomic proportion of magnesium into *o*-bromobenzylmagnesium bromide, which when treated with chloromethyl methyl ether gave 2-*o*-bromophenylethyl methyl ether (VII). This


(VI.) (VII.) (VIII.) (IX.) (X.) (XI.)

compound was converted into a Grignard reagent by the entrainment method using activated magnesium, and this reagent with diethylchlorophosphine, furnished diethyl-(*o*-2-methoxyethylphenyl)phosphine (VIII), as a colourless liquid which was characterised by the preparation of its crystalline methiodide and its dibromopalladium derivative $[(C_{13}H_{21}OP)_2PdBr_2]$.

The phosphine (VIII), when treated in boiling acetic acid solution with hydrogen bromide, undoubtedly first gave the hydrobromide of diethyl-(*o*-2-bromoethylphenyl)phosphine (IX) without immediate cyclisation. The evidence for the existence of this intermediate is similar to that for the corresponding compound in Beeby and Mann's synthesis (*loc. cit.*), namely, that, when the acetic acid had been evaporated under reduced pressure, treatment of the water-soluble residue with sodium hydrogen carbonate liberated an oil. This oil was insoluble in water but dissolved readily in chloroform with evolution of heat and the formation of the water-soluble 1 : 1-diethylphosphindolinium bromide (X); the oil therefore was the uncyclised tertiary phosphine corresponding to the hydrobromide (IX), and on dissolution in chloroform underwent exothermic cyclisation to the phosphonium bromide (X), which could then be readily re-extracted with water.

The aqueous extract thus obtained, when treated with sodium picrate, deposited 1 : 1-diethylphosphindolinium picrate, which after recrystallisation was converted into the corresponding chloride. The latter when heated gave a distillate consisting of 1-ethylphosphindoline and its hydrochloride, undoubtedly with the simultaneous liberation of ethylene : this distillate, when made alkaline and worked up in the usual way, gave 1-ethylphosphindoline (XI) as a colourless liquid, b. p. 104—106°/13 mm., which was readily oxidised on exposure to air. The phosphine was characterised by the preparation of various derivatives : in particular, its crystalline

ethiodide was converted into the ethopicrate, which was identical with that employed for the preparation of the phosphindolinium chloride. It is clear therefore that the destructive distillation of the latter had left the ring system unchanged.

We are now investigating the use of phenylphosphine, $Ph{\cdot}PH_2$, for the synthesis of the corresponding *iso*phosphindolines and other cyclic derivatives of phosphorus.

Experimental.

2-o-Bromophenylethyl Methyl Ether (VII).—The preparation of this Grignard reagent and its treatment with chloromethyl ether were performed in an atmosphere of nitrogen. A solution of *o*-bromobenzyl bromide (250 g.) in ether (570 c.c.) was added with stirring to magnesium (25·1 g., 1·03 atoms) under ether (75 c.c.) during 3 hours; a crystal of iodine was added to start the reaction, which was then controlled as usual to prevent ebullition of the ether. The solution was then stirred for 2 hours at room temperature, cooled to 0—5°, and vigorously stirred whilst chloromethyl ether (80·5 g., 1 mol.) in ether (100 c.c.) was added dropwise during 1 hour. Stirring was continued for a further 3 hours, the mixture being allowed to attain room temperature meanwhile, and a solution of sulphuric acid (85 c.c.) in water (1 l.) being then added.

The ethereal layer was separated, washed with sodium hydrogen carbonate solution, dried, and distilled; fractionation gave 2-*o*-*bromophenylethyl methyl ether* (VII) as a colourless liquid, b. p. 64—67°/0·7 mm., having a pleasant odour (Found: C, 49·9; H, 4·8; Br, 37·1. $C_9H_{11}OBr$ requires C, 50·2; H, 5·1; Br, 37·2%) (98 g., 46%). A small fraction, b. p. 170—190°/0·02 mm., gave 2 : 2′-dibromodibenzyl, m. p. 84° (alone and mixed) (cf. Beeby and Mann, *loc. cit.*).

Diethyl-(o-2-methoxyethylphenyl)phosphine (VIII).—This preparation was carried out under nitrogen with activated magnesium (Holliman and Mann, *J.*, 1942, 739). A solution of the ether (VII) (21·5 g.) and ethyl bromide (5·5 g., 0·5 mol.) in ether (70 c.c.) was added to magnesium (3·83 g., 1·58 atoms) under ether (20 c.c.) at such a rate that the ether boiled gently. The complete mixture was then boiled under reflux for 3 hours, cooled, and chilled in ice-water whilst a solution of diethylchlorophosphine (12·5 g., 1 mol.) in benzene (70 c.c.) was added dropwise with vigorous stirring. The mixture was then boiled for 2 hours, cooled, and hydrolysed with aqueous ammonium chloride. The organic layer, when separated, dried, and distilled, gave the phosphine (VIII) as a colourless oil, b. p. 119—133°/26 mm. (15 g., 67%). The phosphine frothed so persistently on distillation that complete purification was not attempted. It gave a *methiodide*, colourless crystals after recrystallisation from methyl iodide and of m. p. 95·5—96° (Found: C, 45·9; H, 6·3. $C_{14}H_{34}OIP$ requires C, 45·9; H, 6·55%), and also, when treated with an alcoholic solution of potassium palladobromide, *dibromobis[diethyl-(o-2-methoxyethylphenyl)phosphine]-palladium*, orange crystals (from alcohol), m. p. 178° (Found: C, 43·8; H, 5·6. $C_{28}H_{42}O_2Br_2P_2Pd$ requires C, 43·7; H, 5·9%).

1 : 1-*Diethylphosphindolinium Picrate.*—A mixture of acetic acid (250 c.c.) and hydrobromic acid (constant b. p.; 250 c.c.) was saturated with hydrogen bromide, added to the phosphine (VIII) (15 g.), and then boiled under reflux for 3 hours whilst a current of hydrogen bromide was passed through. The solvent was removed under reduced pressure, and the residue treated with an excess of sodium hydrogen carbonate solution. The mixture was shaken vigorously with chloroform, which became warm. The aqueous layer when treated with sodium picrate solution deposited the yellow phosphindolinium picrate; a further crop was obtained by evaporation of the chloroform, and treatment of an aqueous solution of the residue with sodium picrate. The united crops after crystallisation from alcohol gave the *picrate* (8·25 g., 29%), as yellow crystals, m. p. 145—145·5° (Found: C, 51·0; H, 4·4; N, 9·9. $C_{18}H_{20}O_7N_3P$ requires C, 51·3; H, 4·75; N, 10·0%).

1-*Ethylphosphindoline* (XI).—The picrate (7 g.) was decomposed with hydrochloric acid, the picric acid extracted with ether, and the aqueous solution evaporated under reduced pressure. The residual chloride (as X), which slowly crystallised, was thoroughly dried and then decomposed by being heated at 350—370°/12 mm. in a nitrogen atmosphere. The viscous semi-crystalline distillate, consisting of the phosphine (XI) and its hydrochloride, was treated with aqueous sodium hydrogen carbonate solution, and the liberated phosphine extracted with benzene. The dried extract on fractionation in a nitrogen atmosphere gave the *phosphine* (XI) (2 g., 75%) as a colourless liquid, b. p. 104—106°/13 mm. (Found: C, 73·7; H, 8·0. $C_{10}H_{13}P$ requires C, 73·2; H, 7·9%). The phosphine has an odour closely resembling that of 1-ethyl-1 : 2 : 3 : 4-tetrahydrophosphinoline and readily darkens on exposure to air.

The phosphine combined with ethyl iodide to give 1 : 1-*diethylphosphindolinium iodide* (as X), colourless crystals, m. p. 123°, after recrystallisation from light petroleum (b. p. 80—100°) containing a small proportion of alcohol (Found: C, 45·1; H, 5·4. $C_{12}H_{18}IP$ requires C, 45·0; H, 5·6%). A sample of this iodide gave the corresponding picrate, identical with that employed for the preparation of the chloride. Treatment of the phosphine with potassium palladobromide furnished *dibromobis-1-ethylphosphindolinepalladium*, which separated from alcohol as pale yellow crystals of the *alcoholate*, m. p. 147° (Found: C, 41·1; H, 4·95. $C_{20}H_{26}Br_2P_2Pd,C_2H_6O$ requires C, 41·2; H, 5·0%); at 85°/0·2 mm. for 6 hours this gave the solvent-free *compound* of unchanged m. p. (Found: C, 40·4; H, 4·6. $C_{20}H_{26}Br_2P_2Pd$ requires C, 40·4; H, 4·4%).

We gratefully acknowledge a grant provided by the Department of Scientific and Industrial Research (I. T. M.).

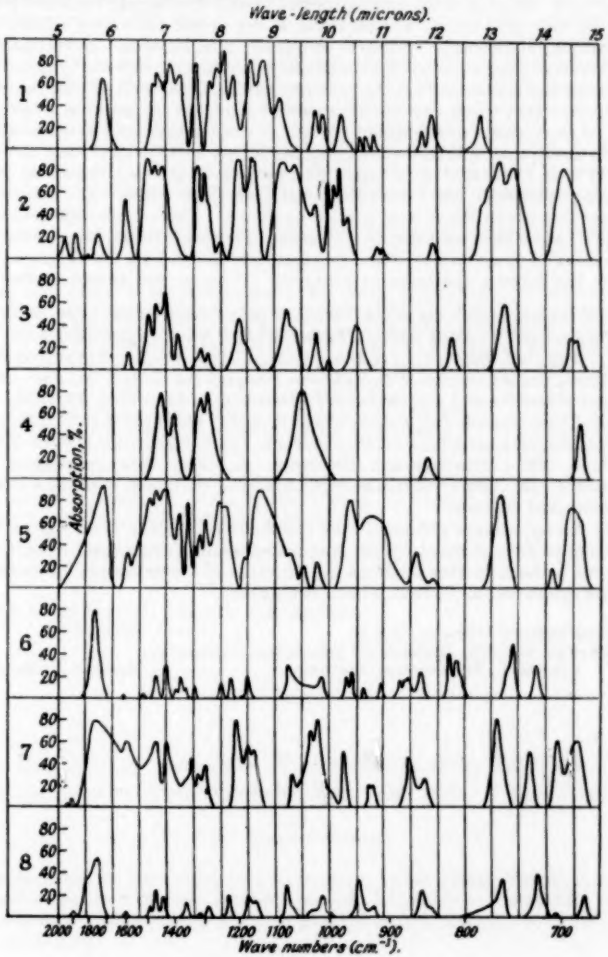
University Chemical Laboratory, Cambridge. [*Received, May 10th,* 1951.]

481. *The Infra-red Spectra of Three Sydnones and Certain N-Nitroso-compounds.*

By J. C. Earl, R. J. W. Le Fèvre, A. G. Pulford, and A. Walsh.

Present work.—Percentage absorptions of eight compounds listed below have been determined from 2 to 15 μ. by using the Perkin–Elmer model 12B recording infra-red spectrometer :

Compound and state.	Curve no. on Fig.
N-Nitrosotriacetonamine, as solidified layer	1
N-Nitrosodiphenylamine, as solidified layer	2
N-Nitrosomethylaniline, as liquid	3
N-Nitrosodimethylamine, as liquid	4
N-Nitrosophenylglycine, as suspension in Nujol	5
N-β-Naphthylsydnone, as suspension in Nujol	6
C-Bromo-*N*-phenylsydnone, as suspension in Nujol	7
N-Phenylsydnone, as suspension in Nujol	8



Comment.—In various *N*-nitrosoamides the –CO–N–N=O unit has been characterised by bands around 1490 and 1720 cm.$^{-1}$, ascribed respectively to >N–N=O and >C=O (cf. " The Chemistry of Penicillin," Princeton Univ. Press, 1949, pp. 152, 177).

Colthup (*J. Opt. Soc. Amer.*, 1950, **40**, 397) however assigns the absorption of the nitroso-group to the region 1310—1420 cm.$^{-1}$. From the Fig. it is seen that compounds 1—5 show absorption in common at *ca.* 1400 cm.$^{-1}$. Since Barredo and Goubeau (*Z. anorg. Chem.*, 1943, **251**, 2) and Wittek (*Anzeiger Akad. Wiss. Wien*, 1943, **3**, 5) have reported a Raman line at 1405 cm.$^{-1}$ for $Me_2N{\cdot}NO$ we relate this frequency to the *N*-nitroso-group in our substances. The non-occurrence of any such absorption with *N*-phenylsydnone (curve 8), and its weakness with the other two sydnones (curves 6 and 7), are of interest because hitherto the only evidence for the disappearance of the nitroso-group has been the failure of sydnones to respond to the qualitative Liebermann test (Earl and Mackney, *J.*, 1935, 899) and the general absence in the sydnones of chemical behaviour usually found in nitroso-compounds.

Curves 6—8 display strong absorptions at 1766, 1756, 1752 cm.$^{-1}$; these correspond approximately with the values listed by Hartwell, Richards, and Thompson (*J.*, 1948, 1436) for the " ester-carbonyl " group, and the maxima observed with the phenylglycine and triacetonamine derivatives (1722 and 1719 cm.$^{-1}$; curves 1 and 5) are nearer the values reported by the last authors for " carboxylic-carbonyl " group or simple aliphatic ketones. Nevertheless deductions regarding the states of these carbonyl groups might be dangerous since the sydnones are believed to contain a novel and resonating heterocyclic nucleus, and Hartwell, Richards, and Thompson (*loc. cit.*) have noted that where the >C=O is part of a ring its frequency is a complex function of ring-strain, of the natures of side-chain groups, of conjugation, and of other factors. Since the appropriate absorption in liquid *cyclo*pentanone occurs at 1744 cm.$^{-1}$, and in *cyclo*hexanone or acetone at 1714 or 1718 cm.$^{-1}$ respectively (Hartwell *et al.*, *loc. cit.*) ring-strain *alone* seems to cause an increase of some 30 cm.$^{-1}$ from the usual open-chain value. The effects of the other factors are unpredictable on the data at present available. Thus, while high >C=O frequencies (up to 1820 cm.$^{-1}$) have been recorded by Woodward (*J. Amer. Chem. Soc.*, 1950, **72**, 3327) for certain oxazolones and $\beta\gamma$-unsaturated five-ring lactones, contrarily a low frequency (1664 cm.$^{-1}$) is indicated by the Raman spectrum of antipyrin (Taboury and Boureau, *Bull. Soc. chim.*, 1945, [v], **12**, 594)—a molecule in which carbonyl polarisation of the type $>C\overset{\curvearrowright}{=}O$ is evident from other directions (cf. *J.*, 1949, 2812). In the light of previous discussions (cf. particularly, *J.*, 1948, 2269; 1949, 103, 307, 746; *J. Chim. physique*, 1949, **46**, 244) on the sydnones, coupled with the considerations set out by Walsh (*Trans. Faraday Soc.*, 1947, **43**, 158; *Ann. Reports*, 1947, **44**, 45) and Schneider and Halverstadt (*J. Amer. Chem. Soc.*, 1948, **70**, 2626), we expected at the outset that their ketonic frequencies would probably resemble that in antipyrin. At the same time, the absorptions observed (1750—1770 cm.$^{-1}$) are sufficiently low (cf. Thompson and Linnett, *J.*, 1937, 1291; Drayton and Thompson, *J.*, 1948, 1416) to suggest insignificant contributions of the keten-like structure already dismissed by Baker, Ollis, and Poole (*J.*, 1949, 307) on stereochemical grounds.

Incidentally the appearance of a regular ketonic band in *N*-nitrosophenylglycine, considered against the results of Slovochotova, Sirkin, and Volkenstein (*Compt. rend. Acad. Sci. U.R.S.S.*, 1942, **35**, 146) for betaine, further confirms the rejection of " zwitterion " formulations for the precursors of the sydnones (cf. *J.*, 1948, 2269; 1949, 5103).

UNIVERSITY OF SYDNEY, SYDNEY, N.S.W.,
CHEMICAL PHYSICS SECTION, DIVISION OF INDUSTRIAL CHEMISTRY,
C.S.I.R.O., MELBOURNE, VICTORIA.
[*Received, October 28th*, 1950.]

482. *Trichloromethylamine (Aminochloroform).*

By K. R. Simon Ascher.

There is no reference in the literature to a successful synthesis of trichloromethylamine (aminochloroform), though several unsuccessful attempts to prepare it have been recorded: (1) Spiegel and Spiegel (*Ber.*, 1907, **40**, 1733) attempted to prepare it by a Curtius reduction, but as they failed to obtain trichloroacetazide they concluded that the radicals $\cdot N_3$ and $\cdot CCl_3$ are incompatible. (2) Reduction of chloropicrin also failed: among the reducing agents used were stannous chloride and hydrochloric acid (Raschig, *Ber.*, 1885, **18**, 3326), iron and acetic acid (Geisse, *Annalen*, 1859, **109**, 282), iron filings and dilute hydrochloric acid (Frankland *et al.*, *J.*, 1919, **115**, 161), and potassium pyrosulphite (Geisse, *loc. cit.*).

Two workers may have encountered trichloromethylamine during their work, but they do not state the fact explicitly. Henderson and Macbeth (*J.*, 1922, **121**, 892) found, but without recording experimental details, that: "hydrazine removes one of the chlorine atoms from chloropicrin very slowly in the cold. Potassium ferrocyanide is without action. *Titanous chloride reduces the nitro-group, but leaves the halogen unattacked.*" Piutti (*Gazzetta*, 1921, **51**, I, 145) stated that solutions of chloropicrin in methyl alcohol or ethyl alcohol separate after one day into two layers with precipitation of ammonium chloride, and assumed that the alcohols reduce the nitro- to an amino-group, which is then split off as ammonia.

There appears to be no reference to a synthesis of $NH_2 \cdot CHX_2$ and $NH_2 \cdot CH_2X$ (X = halogen), but Hinkel and Watkins (*J.*, 1944, 647) inferred from the final products of the reaction between hydrogen chloride and hydrogen cyanide that dichloromethylamine appears as an intermediate product in the *reaction*.

It was found that trichloromethylamine could be obtained by a slightly modified Hofmann degradation.

Experimental.—To 16·5 g. of trichloroacetamide are added, with cooling and stirring, 16 g. (5·2 ml.) of bromine, followed by cold aqueous potassium hydroxide (40 g. in 280 ml.) until the colour of the solution turns from a red-brown to a bright yellow. Then the solution is poured into aqueous potassium hydroxide (16 g. in 30 ml.) previously heated to 70—75°. The solution becomes strongly opalescent and is kept at 70—75° until the yellow colour disappears (*ca.* 1 minute). Then, *immediately*, the solution is cooled in ice, after which it is extracted many times with small quantities of ether (until it clears). The ethereal extract is dried (Na_2SO_4), and the ether allowed to evaporate in a large porcelain dish at room temperature. The residue, when further dried in a desiccator over phosphoric oxide, affords a viscous oil (yield, 10%), with a smell resembling that of carbon tetrachloride. *Trichloromethylamine* (Found: N, 10·3; Cl, 79·0. CH_2NCl_3 requires N, 10·4; Cl, 79·2%) has b. p. 109° and is not inflammable. It is strongly acidic, owing to the inductive influence of the chlorine atoms on the hydrogen (cf. nitramine), and reacts with aqueous silver nitrate to give the compound $NHAg \cdot CCl_3$, which is insoluble in concentrated ammonium hydroxide. Trichloromethylamine seems to possess some ovicidal properties against eggs of *Pediculus humanus corporis* (body louse).

Use of hypochlorite instead of hypobromite leads to a violent reaction, with evolution of ammonia, and no trichloromethylamine is produced.

Malaria Research Station, Hebrew University,
Rosh-Pinna, Israel.

[*Received, December 18th*, 1950.]

---

483. *The Reaction of Aromatic Hydrocarbons with Lithium Aluminium Hydride, and a New Technique for the Use of the Reagent.*

By Isaac Goodman.

It is known (Goodman, *J.*, 1951, 846) that anthracene, unlike phenanthrene, is reduced to the dihydro-compound by reaction with lithium aluminium hydride at about 220°, and it was of interest to examine whether the reduction of other aromatic hydrocarbons could be effected under milder conditions.

When lithium aluminium hydride is warmed with " Carbitol," a slow evolution of hydrogen commences at about 70° and at 90—95° a violent reaction ensues, which, if suitably controlled, yields a clear colourless solution possessing powerful reducing properties; thus it reduces acenaphthylene to acenaphthene. The reaction with " Carbitol " presumably yields an alkoxide form of the elements of the reagent, either as a complex compound or as a mixture of metal alkoxides (cf. Solms, *Chimia*, 1951, **5**, 25; Krajkeman, *Mfg. Chem.*, 1951, **22**, 147); it is noteworthy, however, that although the hydride dissolves readily in *n*-butanol, the resulting solution does not reduce acenaphthylene.

Advantages of the new reagent are: (*a*) it presents a stable reducing agent at temperatures up to the boiling point of " Carbitol " (approximately 200°), and (*b*) the vigorous reaction generally obtained in the hydrolysis of the excess of lithium aluminium hydride is avoided.

Dilution of the " Carbitol " reagent with water precipitates the metal hydroxides without evolution of heat; reaction with hydrocarbons followed by direct hydrolysis with dilute acid gives the reaction-product as a precipitate free from other organic matter.

Unless great care is exercised in the preparation of the reagent, the reaction above 90° becomes uncontrollably violent, particles of the hydride becoming incandescent and causing considerable carbonisation. To avoid this the reaction must be conducted in nitrogen, and the hydride used as a very fine powder with suitable agitation, and cooling when necessary. The reagent should be prepared in a considerable excess of " Carbitol."

Addition of acenaphthylene to the " Carbitol " reagent resulted in the immediate, almost quantitative reduction to acenaphthene, whereas acenaphthylene was recovered unchanged (in 95% yield) after being heated under reflux with the hydride in ether for 5 hours. Anthracene was recovered unchanged (in 97% yield) after being heated for 3 hours with the " Carbitol "–lithium aluminium hydride reagent at the boiling point of the solvent (cf. the " dry " reaction which gave a 56% yield of dihydroanthracene at substantially the same temperature). Pyrene, which is not reduced in ether solution by the hydride, was similarly recovered unchanged in the " Carbitol " method. Naphthacene, pentacene, and perylene were equally not reduced by the " Carbitol "–hydride reagent or by the solid reagent in boiling naphthalene solution. 9 : 9′-Difluorenylidene was reduced in ether solution to 9 : 9′-difluorenyl, the same product also being obtained when difluorenylidene was refluxed in ethanol with Raney nickel (cf. Mozingo, Spencer, and Folkins, *J. Amer. Chem. Soc.*, 1944, **66**, 1859).

The formation of the dihydro-compound when anthracene was heated with lithium aluminium hydride above the decomposition temperature of the latter remains the sole example of the reduction of an aromatic ring by this reagent, and it is probable that such rings are indeed immune to lithium aluminium hydride, and that the reduction of anthracene is a heterogeneous reaction brought about by liberated hydrogen on a catalytic surface made available during the decomposition of the reagent.

Reduction of Acenaphthylene to Acenaphthene.—(i) *Pre-formation of the reagent.* " Carbitol " (50 c.c.) and lithium aluminium hydride (1 g.) were warmed, the precautions already described being observed. At 95° a violent reaction began, with spontaneous rise of temperature to 120°. Acenaphthylene (1 g.) in " Carbitol " (10 c.c.) was added to the cooled solution, the yellow colour being immediately discharged. The mixture was warmed for 15 minutes at 100° and then hydrolysed. The product (0·85 g.) formed very pale yellow crystals, m. p. 88—93°, from ethanol.

(ii) *Without pre-formation of the reagent.* Acenaphthylene (1 g.) and finely powdered lithium aluminium hydride (1 g.) were warmed at 120° for 3 hours in " Carbitol " (20 c.c.); during this period a quantity of dark grey inorganic solid agglomerated at the bottom of the reaction mixture. Decomposition with dilute hydrochloric acid did not cause any temperature increase. The greyish product (97%) was crystallised from ethanol, giving acenaphthene (0·8 g.), m. p. 89—93°.

The thermal equilibrium diagram for the system acenaphthene–acenaphthylene (Kynaston and Idris Jones, *J. Soc. Chem. Ind.*, 1949, **68**, 228) permitted both products to be determined as acenaphthene of 96% purity (confirmed by the melting-point depression obtained when very small quantities of acenaphthylene were added).

[ADDED, May 6th, 1951.] *Reduction of 9 : 9′-Difluorenylidene to 9 : 9′-Difluorenyl.*—(i) *With lithium aluminium hydride.* The hydrocarbon (0·05 g.) and lithium aluminium hydride (0·5 g.) were refluxed in ether (30 c.c.) for 5½ hours. The solution was decomposed with dilute sulphuric acid, and the product isolated from the ethereal layer as a yellow solid, m. p. 224—232°. Crystallisation from *n*-butanol gave needles of 9 : 9′-difluorenyl (0·039 g., 77·5%), m. p. 241—242° (cf. de la Harpe and van Dorp, *Ber.*, 1875, **8**, 1049; Wanscheid, *J. Russ. Phys. Chem. Soc.*, 1926, **58**, 252, 280, 282).

(ii) *With Raney nickel.* Raney nickel (from 40 g. of the alloy) was washed with water until the wash-liquor pH fell to 9·5. The water was decanted, and absolute ethanol (100 c.c.) and 9 : 9′-difluorenylidene

(1 g.) added. After 4 hours' refluxing the red colour of the hydrocarbon had disappeared. Evaporation of the solution gave 9 : 9'-difluorenyl (0·2 g.), m. p. 237—240° raised by crystallisation from butanol (charcoal) to 242°.

The author is indebted to Mr. W. F. Maddams of the Physics Department, Manchester Oil Refinery, Ltd., who kindly made available samples of naphthacene, pentacene, and perylene.

PETROCARBON LTD., RESEARCH LABORATORIES,
TWINING ROAD, MANCHESTER, 17.
(present address) IMPERIAL CHEMICAL INDUSTRIES LIMITED,
RESEARCH LABORATORIES, HEXAGON HOUSE,
MANCHESTER, 9.

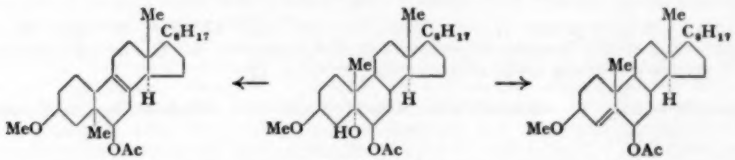
[*Received, March 9th*, 1951.]

---

484. *The Dehydration of 6β-Acetoxy-3β-methoxycholestan-5α-ol.*

By M. DAVIS and V. PETROW.

THE constitution 6β-acetoxy-3β-methoxycholest-4-ene (III) previously assigned (Petrow, *J.*, 1937, 1077) to the product obtained by dehydrating 6β-acetoxy-3β-methoxycholestan-5α-ol (II) with sulphuric acid–acetic anhydride, requires revision in the light of subsequent work.



We find that the properties of the foregoing dehydration product are more consistent with its formulation as a 6β-acetoxy-3β-methoxy-5-methyl-19-norcholest-8(9)-ene (I) than as (III). Thus the compound is unsaturated towards tetranitromethane. It fails to give a colour with the trichloroacetic acid reagent, but gives a typical green colour in the Tortelli–Jaffé reaction (cf. Petrow, Rosenheim, and Starling, *J.*, 1938, 677). It shows a high positive rotation, retained in the 6-hydroxy-compound, but changed in sign in the 6-keto-derivative (cf. Davis and Petrow, *J.*, 1949, 2973). The conclusion that the compound belongs to the " Westphalen " series thus appears to be inescapable.

Additional evidence supporting this view is that dehydration of (II) with thionyl chloride–pyridine (cf. Petrow, Rosenheim, and Starling, *loc. cit.*) gives a new compound, isomeric with (I), which gives a blue colour with trichloroacetic acid and is thus the authentic 6β-acetoxy-3β-methoxycholest-4-ene (III).

Experimental.—M. p.s are corrected. Optical rotations were measured in chloroform solution. Microanalyses are by Drs. Weiler and Strauss, Oxford.

6β-Acetoxy-3β-methoxycholest-4-ene (III). Redistilled thionyl chloride (0·2 ml.) was added to a solution of 6β-acetoxy-3β-methoxycholestan-5α-ol (1 g.) (Petrow, *loc. cit.*) in dry pyridine (5 ml.). After 1·5 hours at room temperature the solution was poured into water. *6β-Acetoxy-3β-methoxycholest-4-ene* (0·9 g.) separated and crystallised from methanol as needles, m. p. 93—94° (Found : C, 78·5; H, 10·6. $C_{32}H_{56}O_3$ requires C, 78·5; H, 11·0%). *3β-Methoxycholest-4-en-6β-ol*, obtained by hydrolysis of the acetate with ethanolic potassium hydroxide, crystallised from alcohol as needles, m. p. 171—173° (Found : C, 79·4; H, 11·3. $C_{28}H_{48}O_2,\frac{1}{2}H_2O$ requires C, 78·9; H, 11·6%).

6-Acetoxy-3-methoxy-5-methyl-19-norcholest-8(9)-ene (I) was prepared in 48—52% yield by dehydration of 6β-acetoxy-3β-methoxycholestan-5α-ol with potassium hydrogen sulphate–acetic anhydride. (cf. Petrow, *J.*, 1939, 998). Hydrolysis with 5% ethanolic potassium hydroxide gave *3-methoxy-5-methyl-19-norcholest-8(9)-en-6-ol*, which separated from aqueous alcohol as needles, m. p. 108°, $[\alpha]_D^{14}$ +119·4° ± 0·6° (*c*, 1·575) (Found : C, 80·6; H, 11·8. $C_{28}H_{48}O_2$ requires C, 80·8; H, 11·6%). The *6-benzoyl* derivative, prepared by boiling the hydroxy-compound with benzoyl chloride in pyridine for 1 hour, formed fine needles, m. p. 91—92°, from acetone–methanol (Found : C, 80·4; H, 10·0. $C_{35}H_{52}O_3$ requires C, 80·7; H, 10·1%).

3-*Methoxy-5-methyl*-19-*norcholest*-8(9)-*en*-6-*one*. 3-Methoxy-5-methyl-19-norcholest-8(9)-en-6-ol (1 g.) in benzene (10 ml.) was shaken for 5 hours at room temperature with chromium trioxide (0·33 g.) in 70% acetic acid (15 ml.). The neutral fraction of the product, when crystallised from acetone–methanol, yielded **3-*methoxy-5-methyl*-19-*norcholest*-8(9)-*en*-6-*one*** (50—55%) in feathery needles, m. p. 65—66°, $[\alpha]_D^{14}$ −4·6° ± 0·8° (*c*, 1·310) (Found: C, 81·3; H, 10·9. $C_{32}H_{44}O_2$ requires C, 81·1; H, 11·2%). The 2 : 4-***dinitrophenylhydrazone***, m. p. 125—127°, crystallised from chloroform–methanol (Found: N, 9·1. $C_{44}H_{50}O_8N_4$ requires N, 9·4%).

3-*Methoxy-5-methyl*-19-*norcholest*-8(9)-*en*-6-*yl sulphite*. A solution of 3-methoxy-5-methyl-19-norcholest-8(9)-en-6-ol (0·1 g.) in pyridine was treated with thionyl chloride (0·1 ml.) and kept at room temperature for 24 hours. The ***sulphite*** obtained by pouring the mixture into water and extraction with ether separated from acetone as needles, m. p. 191° (Found: C, 76·6; H, 10·8; S, 3·45. $C_{56}H_{94}O_5S$ requires C, 76·5; H, 10·8; S, 3·6%).

One of us (M. D.) thanks the Department of Scientific and Industrial Research for a maintenance allowance.

QUEEN MARY COLLEGE, LONDON, E.1.
RESEARCH LABORATORIES,
THE BRITISH DRUG HOUSES, LTD., N.1.

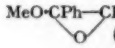
[*Received, April 13th*, 1951.]

---

485. *The Formation of Osazones. Part III.**

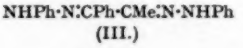
By G. J. BLOINK and K. H. PAUSACKER.

TEMNIKOVA and KROPAČEVA (*J. Gen. Chem., U.S.S.R.*, 1949, **19**, 1917; cf. *Chem. Abs.*, 1950, **44**, 1929) claim that 1 : 2-epoxy-1-methoxy-1-phenylpropane (I) reacts with phenylhydrazine, in ethyl alcohol containing acetic acid, to form (II), m. p. 126°.



(I.)

NHPh·N:CPh·CHMe·NH·NHPh
(II.)



(III.)

This result is unusual for it would be expected that (II) would be converted into 1-phenyl-1 : 2-di(phenylhydrazono)propane (III), m. p. 105°, which has previously been prepared by Müller and von Pechmann (*Ber.*, 1889, **22**, 2127). Compounds similar to (II) have previously been postulated only as labile intermediates in osazone formation (cf. Weygand and Reckhaus, *Ber.*, 1949, **82**, 442), it being assumed that they are readily oxidised by phenylhydrazine.

Repetition of Temnikova and Kropacheva's work gave a compound, m. p. 128°, which was identical (mixed m. p.) with 1-acetyl-2-phenylhydrazine (Found: C, 64·0; H, 6·4; N, 18·7. Calc. for $C_8H_{10}ON_2$: C, 64·0; H, 6·7; N, 18·7%). Fischer (*Annalen*, 1878, **190**, 270) gives m. p. 128·5°; Andeslini (*Ber.*, 1891, **24**, 1993, footnote) has shown that phenylhydrazine is readily acetylated, even in aqueous acetic acid, so that the compound assigned structure (II) is therefore 1-acetyl-2-phenylhydrazine.

When *p*-chlorophenylhydrazine reacted with (I) under the same conditions, colourless crystals of 1-acetyl-2-*p*-chlorophenylhydrazine, m. p. 157°, were isolated (Found: C, 51·6; H, 4·9; N, 15·3. Calc. for $C_8H_9ON_2Cl$: C, 52·0; H, 4·9; N, 15·2%). Von Pechmann and Vanino (*Ber.*, 1894, **27**, 224) give m. p. 154°. When 1-phenylpropane-1 : 2-dione was condensed with *p*-chlorophenylhydrazine, yellow needles of **1 : 2-*di*-(p-*chlorophenylhydrazono*)-1-*phenylpropane*** were formed; after crystallisation from ethanol they had m. p. 157° (mixed m. p. with 1-acetyl-2-*p*-chlorophenylhydrazine 139°) (Found: C, 63·1; H, 4·9; N, 13·8; Cl, 18·3. $C_{21}H_{20}N_4Cl_2$ requires C, 63·1; H, 5·0; N, 14·0; Cl, 17·8%).

It is thus apparent that hydrazino-hydrazones, such as (II), are not formed when (I) reacts with phenylhydrazines.

Microanalyses are by Dr. W. Zimmermann.

UNIVERSITY OF MELBOURNE, N.3, VICTORIA, AUSTRALIA.

[*Received, April 16th*, 1951.]

---

* Part II, *J.*, 1951, 622.

486. *The Bromination of o-Acylaminotoluenes. A Correction.*

By D. G. I. Felton.

Leulier and Arnoux (*Bull. Soc. chim.*, 1930, **47**, 730; see also Leulier, *ibid.*, 1924, **35**, 1325; 1926, **39**, 29; Leulier and Pinet, *ibid.*, 1927, (4), **41**, 1362), in the course of the formers' study of halogenation by means of hydrogen halide–aqueous hydrogen peroxide, reported that treatment of *o*-acetamidotoluene with hydrobromic acid and perhydrol yielded 2-acetamido-5-bromotoluene as needles, m. p. 156—157°, whereas the same reagents with *o*-benzamidotoluene afforded 2-benzamido-6-bromotoluene, m. p. 175—176°. This surprising implication of a variation in the directive influence of an acylamino-group depending upon the acyl group, on which Leulier and Arnoux did not even comment, warranted further examination. The French workers did not prove the orientation of their products chemically, but relied on a comparison of the melting points with those quoted in the literature :

Toluene.	M. p.	Reference.
2-Acetamido-5-bromo-	156—157°	Bogert and Hand, *J. Amer. Chem. Soc.*, 1905, **27**, 1479.
2-Acetamido-6-bromo-	154—155	Cohen and Miller, *J.*, 1904, **85**, 1627.
	158	Noelting, *Ber.*, 1904, **37**, 1022.
2-Benzamido-5-bromo-	115	Ressy and Ortodocsu, *Bull. Soc. chim.*, 1923, (4), **33**, 639.
2-Benzamido-6-bromo-	176—177	Cohen and Miller, *loc. cit.*

The orientation of all of these compounds had been rigorously established except that of 2-benzamido-5-bromotoluene, which Ressy and Ortodocsu had prepared by bromination of *o*-benzamidotoluene in acetic acid solution by bromine.

On investigation, the observations of Leulier and Arnoux were confirmed, and the bromo-derivatives of *o*-acetamido- and *o*-benzamido-toluenes were found to melt at 157—158° and 174—175°, respectively. However, hydrolysis of 2-benzamido-*x*-bromotoluene with 70% sulphuric acid, followed by acetylation of the isolated amine, yielded 2-acetamido-*x*-bromotoluene, m. p. 159—160°, undepressed on admixture with the bromo-derivative obtained from *o*-acetamidotoluene by the method described by Leulier and Arnoux. Thus these authors' suggestion of a variation in the directive influence of an acylamino-group was not sustained.

However, there still remained the orientation of the bromine atom, especially in view of the close correspondence in the melting points of the 5- and the 6-bromo-derivative of *o*-acetamidotoluene. It seemed unlikely that bromination could occur in any position other than *p*- to the acylamino-group. Accordingly, the bromination of *o*-benzamidotoluene was repeated following the directions given by Ressy and Ortodocsu (*loc. cit.*), whereupon a bromo-derivative, m. p. 174—175°, was isolated, the m. p. of which was undepressed by Leulier and Arnoux's bromo-compound. Apparently the m. p. 115° quoted in the literature is a typographical error. The possible confusion of m. p.s was now complete. Both the 5- and the 6-bromo-derivative of *o*-acetamidotoluene melt at the same temperature and the same now appears true of the derivatives of *o*-benzamidotoluene. For a rigorous orientation, the 2-acetamido-*x*-bromotoluene was oxidised by potassium permanganate in aqueous magnesium sulphate at 80—85° to the corresponding benzoic acid, m. p. 219—221° [cf. 2-acetamido-5-bromobenzoic acid, m. p. 223—224° (Bogert and Hand, *loc. cit.*); 2-acetamido-6-bromobenzoic acid, m. p. 224° (Friedländer, Bruckner, and Deutsch, *Annalen*, 1912, **388**, 30)], and this was deacetylated by refluxing it with 50% sulphuric acid yielding *x*-bromoanthranilic acid as needles, m. p. 213—214° (decomp.). This was shown to be identical (mixed m. p.) with 5-bromoanthranilic acid, prepared by Wheeler (*J. Amer. Chem. Soc.*, 1909, **31**, 565) by direct bromination of anthranilic acid dissolved in acetic acid, and orientated by him by deamination *via* the diazonium salt to *m*-bromobenzoic acid.

Consequently, bromination of *o*-acylaminotoluenes with hydrobromic acid and perhydrol, following the directions of Leulier and Arnoux proceeds normally to yield 2-acylamino-5-bromotoluenes.

The author thanks the University of Durham for the award of an I.C.I. Fellowship.

University of Durham, King's College,
Newcastle-on-Tyne, 1.

[*Received, April 23rd*, 1951.]

487. *A New Synthesis of* 4 : 6-*Dihydroxypyrimidines.*

By R. Hull.

Comparatively few pyrimidines unsubstituted in position 2 have been described, and before 1943 these had been synthesised by elimination of a suitable substituent from that position. However, Kenner, Lythgoe, Todd, and Topham (*J.*, 1943, 388) reported that 4 : 6-dihydroxypyrimidine was synthesised from formamidine and diethyl malonate, and later (*J.*, 1943, 574) that the corresponding diamino-compound was formed from ethyl formate and malondiamidine. It is now shown that by substituting malondiamide for malondiamidine in the latter synthesis, the expected 4 : 6-dihydroxypyrimidine is obtained in satisfactory yield. This is the more convenient synthesis of this compound.

Reaction of the diamide and the ester was carried out in the presence of sodium ethoxide, and the product on treatment with phosphoryl chloride gave 4 : 6-dichloropyrimidine, undepressed in melting point on admixture with an authentic specimen (*ibid.*; *J.*, 1943, 575).

The reaction appears to be general, for phenyl- and ethyl-malondiamide which were treated in like fashion gave the corresponding 5-phenyl- and 5-ethyl-4 : 6-dihydroxypyrimidines.

Experimental.—**4 : 6-*Dihydroxypyrimidine.*** Malondiamide (10·2 g.) was added to alcoholic sodium ethoxide (4·6 g. of sodium in 150 c.c. of alcohol), followed by ethyl formate (11·0 g.), and the mixture heated under reflux for 2 hours. Next morning the solid was collected, washed with alcohol, and dissolved in water (50 c.c.). The solution was acidified with 5N-hydrochloric acid, and the solid (4·5 g.) collected. Crystallisation from water gave the product as microprisms, which on being dried became yellow, m. p. >300° (Found: C, 42·75; H, 4·0; N, 25·05. Calc. for $C_4H_4O_2N_2$: C, 42·8; H, 3·6; N, 25·0%).

4 : 6-*Dichloropyrimidine.* 4 : 6-Dihydroxypyrimidine (0·5 g.) was heated under reflux with phosphoryl chloride (7 c.c.) and dimethylaniline (0·26 c.c.) for 3 hours. After cooling, the reaction mixture was poured on ice and extracted with ether. The extract was washed with sodium carbonate solution, dried, and evaporated. The product (0·5 g.) set to yellow needles, m. p. 63·5—64° undepressed by authentic 4 : 6-dichloropyrimidine (*loc. cit.*, p. 575).

4 : 6-*Dihydroxy-5-phenylpyrimidine.* Phenylmalondiamide (8·9 g.) (Dox and Yoder, *J. Amer. Chem. Soc.*, 1922, **44**, 1566) was added to alcoholic sodium ethoxide (2·3 g. of sodium in 75 c.c. of alcohol), followed by ethyl formate (8·05 c.c.), and the mixture was refluxed for 2 hours. After cooling, the solid was digested with warm water (50 c.c.) and filtered from unreacted phenylmalondiamide [2·35 g., m. p. 221—222° (decomp.)], and the filtrate acidified with hydrochloric acid. The pyrimidine (3·55 g.) was collected and washed with a small quantity of water. Crystallisation from water gave microneedles of 4 : 6-*dihydroxy-5-phenylpyrimidine*, m. p. >300° (Found: C, 63·85; H, 4·0; N, 14·85. $C_{10}H_8O_2N_2$ requires C, 63·8; H, 4·25; N, 14·9%).

*5-Ethyl-***4 : 6-*dihydroxypyrimidine.*** Ethylmalondiamide (7·4 g.), alcoholic sodium ethoxide (2·6 g. of sodium in 90 c.c. of alcohol), and ethyl formate (6·3 g.) were refluxed for 2 hours. Next morning the solid was collected, and combined with the residue left after evaporation of the solvent from the filtrate. The combined solids were dissolved in warm water (80 c.c.) and extracted with ether, and the aqueous layer was acidified (hydrochloric acid). The solid (3·3 g.) was collected and washed with water. Crystallisation from water gave prismatic needles of *5-ethyl-***4 : 6-*dihydroxypyrimidine*, m. p. >300° (Found: C, 51·4; H, 5·85; N, 20·0. $C_6H_8O_2N_2$ requires C, 51·4; H, 5·7; N, 20·0%).

Imperial Chemical Industries Limited, Research Laboratories,
Blackley, Manchester, 9.

[*Received, May 9th*, 1951.]

PROCEEDINGS
OF THE
CHEMICAL SOCIETY

OFFICIAL ANNOUNCEMENT

RESEARCH FUND.

A meeting of the Research Fund Committee will be held in November next. All persons who have received grants, and whose accounts have not been declared closed by the Council, are informed that reports must be received by the Society not later than November 1st, 1951.

Applications for grants, to be made on forms obtainable from the General Secretary, must be received on or before November 1st, 1951. Applications from Fellows will receive prior consideration.

Attention is drawn to the fact that the income arising from the donation of the Worshipful Company of Goldsmiths is principally devoted to the encouragement of research in inorganic and metallurgical chemistry, and that the income from the Perkin Memorial Fund is to be applied to investigations relating to problems connected with the coal-tar and allied industries.

PAPERS RECEIVED

(List of papers received between June 18th and July 9th, 1951.)

"The stereochemistry of steroids. Part V. The stereochemical course of the addition of halogens to cholesterol." By D. H. R. BARTON, E. MILLER, and H. T. YOUNG.

"*iso*Quinolines. Part III. The nitration of 3 : 4-dihydro- and 1 : 2 : 3 : 4-tetrahydro-*iso*quinolines." By A. MCCOUBREY and D. W. MATHIESON.

"The electrometric titration of the sodium salts of deoxyribonucleic acids. Part II. The effect of ultrasonic irradiation." By W. A. LEE and A. R. PEACOCKE.

"Potential thiophen chemotherapeutics. Part II. The thiophen analogue of 'Marfanil.'" By J. CYMERMAN and D. FAIERS.

"Polarographic behaviour of iodo-compounds. Part II." By (MRS.) E. GERGELY and T. IREDALE.

"The nature of the co-ordinate link. Part III. Improved preparation of tertiary phosphine, arsine, and stibine complex compounds with platinous chloride." By J. CHATT and R. G. WILKINS.

"Triterpene resinols and related acids. Part XXII. *iso*-β-Amyrenonol and *iso*-β-amyradienonol." By R. BUDZIAREK, J. D. JOHNSTON, W. MANSON, and F. S. SPRING.

"Ethylidene derivatives of mannitol." By E. J. BOURNE, G. T. BRUCE, and L. F. WIGGINS.

"The structure of the product formed from alloxan and *o*-phenylenediamine in the absence of acid." By R. B. BARLOW, H. R. ING, and I. M. LEWIS.

"Mechanism of the formation of dialkyl alkylphosphonates." By W. GERRARD and W. J. GREEN.

"Carcinogenic nitrogen compounds. Part VIII. Further syntheses of hydroxybenzacridines and hydroxydibenzacridines, and problems related thereto." By NG. PH. BUU-HOÏ.

"Anodic syntheses. Part V. Electrolysis of *N*-acylamino-acids. A novel alkoxylation reaction." By R. P. LINSTEAD, B. R. SHEPHARD, and B. C. L. WEEDON.

"Studies in the polyene series. Part XXXIX. Miscellaneous syntheses from ethynyl-*cyclo*hexene of acetylenic compounds related to vitamin A." By H. BADER, B. C. L. WEEDON, and R. J. WOODS.

"Adsorption from binary solutions of completely miscible liquids. Part I. Calculation of surface mole-fraction isotherms." By G. A. H. ELTON.

"The cation-exchange separation of zirconium and hafnium." By B. A. J. LISTER.

"The mechanism of the decarboxylation of substituted malonic acid derivatives." By J. KENYON and W. A. ROSS.

"Partial asymmetric synthesis with α-keto-esters. Part I." By J. A. REID and E. E. TURNER.

"Partial asymmetric synthesis with α-keto-esters. Part II." By D. M. BOVEY and E. E. TURNER.

"Partial asymmetric synthesis with α-keto-esters. Part III." By D. M. BOVEY, J. A. REID, and E. E. TURNER.

"Compounds containing the 2 : 2 : 4-trimethylhexyl skeleton. Part I." By E. E. TURNER and L. TURNER.

"The constitution of yeast ribonucleic acid. Part XIV. The mode of union of the nucleotides." By A. S. ANDERSON, G. R. BARKER, (the late) J. MASSON GULLAND, and M. V. LOCK.

"The electrolytic dissociation of magnesium sulphate and lanthanum ferricyanide in mixed solvents." By H. S. DUNSMORE and J. C. JAMES.

"Physical properties and chemical constitution. Part XXIV. Aliphatic aldoximes, ketoximes, and ketoxime *O*-alkyl ethers, *NN*-dialkylhydrazines, aliphatic ketazines, mono- and di-alkylaminopropionitriles, alkoxypropionitriles, dialkyl azodiformates, and dialkyl carbonates. Bond parachors, bond refractions, and bond-refraction coefficients." By A. I. VOGEL, W. T. CRESSWELL, G. H. JEFFERY and J. LEICESTER.

"The separation of strontium from barium, calcium, and magnesium by partition chromatography on paper." By C. C. MILLER and R. J. MAGEE.

"The separation of potassium, rubidium, and cæsium by partition chromatography on paper." By C. C. MILLER and R. J. MAGEE.

"The separation, detection, and determination of sodium and lithium on paper chromatograms." By C. C. MILLER and R. J. MAGEE.

"Qualitative semimicro-analysis with reference to Noyes and Bray's system. Analysis of the combined alkaline-earth and alkali groups." By C. C. MILLER and R. J. MAGEE.

"The preparation of acid anhydrides." By A. MCGOOKIN and H. PAGE

"Specification of configuration based on enumeration, with reference to the GKD cipher notation." By M. GORDON, C. E. KENDALL, and W. H. T. DAVISON.

"1-Phenylethylamines. Part I. 1-(3-*cyclo*Hexyloxy-4-methoxyphenyl)ethylamines." By A. MCCOUBREY.

"An ultra-filtration method for the optical clarification of protein solutions in light-scattering investigations." By D. A. I. GORING and P. JOHNSON.

"The chemistry of the triterpenes. Part IX. Elucidation of the betulin–oleanolic acid relationship." By G. S. DAVY, T. C. HALSALL, and E. R. H. JONES.

"The chemistry of the triterpenes. Part X. The structures of some isomerisation products from betulin and betulinic acid." By G. S. DAVY, T. G. HALSALL, E. R. H. JONES, and G. D. MEAKINS

"Experiments related to the Strecker degradation." By A. SCHÖNBERG and R. MOUBASHER.

"Syntheses from lupinine." By G. R. CLEMO and J. RUDINGER.

"Amino-acids and peptides. Part V. Determination of L-glutamic acid by the isotope dilution method." By C. C. BARKER, I. W. HUGHES, and G. T. YOUNG.

"The structure of some supposed azetidine-2 : 4-diones. Part I. Derivatives of malonic acid." By F. E. KING, J. W. CLARK-LEWIS, and C. R. P. MORGAN.

"The structures of some supposed azetidine-2 : 4-diones. Part II. Derivatives of tartronic acid." By F. E. KING and J. W. CLARK-LEWIS.

"The structures of some supposed azetidine-2 : 4-diones. Part III. Rudy and Cramer's alloxan 5-*o*-dimethylaminoanil and its alkali hydrolysis product." By F. E. KING and J. W. CLARK-LEWIS.

"The direct oxidation of certain aromatic compounds." By W. P. THISTLETHWAITE.

"A thermochemical evaluation of bond strengths in some carbon compounds. Part II. Bond strengths based on the reaction $CH_3I + HI \longrightarrow CH_4 + I_2$." By R. J. NICHOL and A. R. UBBELOHDE.

"Organic fluoro-compounds. Part V. ω-Trihalogenoacetophenones." By W. B. WHALLEY.

"Organic fluoro-compounds. Part VI. Some trifluoromethylchromones and coumarins." By W. B. WHALLEY

"A new synthesis of lucanthone. ('Miracil D, Nilodin')." By THOMAS M. SHARP.

"Isomers of retinene 2 : 4-dinitrophenylhydrazone." By MARC JULIA and B. C. L. WEEDON.

"Synthesis of fluoranthenes. Part VII. Synthesis of 2 : 3-benzofluoranthene." By H. W. D. STUBBS and S. HORWOOD TUCKER.

"The ultra-violet absorption spectra of phenylpyrimidines." By ALLISON MAGGIOLO and P. B. RUSSELL.

"Carcinogenic nitrogen compounds. Part IX. The use of amino-tetralins for the synthesis of dibenzacridines and related compounds." By NG. PH. LUU-HOÏ and P. JACQUIGNON.

"The synthesis of sugars from simpler substances. Part II. The synthesis of DL-ribose *in vitro* from D-glyceraldehyde and glycollic aldehyde." By L. HOUGH and J. K. N. JONES.

"Synthesis of 2 : 3-benzofluoranthene." By N. CAMPBELL and A. MARKS.

"The potentiometric titration of potassium iodate in acid solution with potassium iodide. The potentiometric titration of potassium iodate in acid solution with potassium iodide." By H. T. S. BRITTON, R. E. COCKADAY, and J. K. FOREMAN.

"A potentiometric study of the reduction of potassium bromate in acid solution with potassium iodide." By H. T. S. BRITTON and H. GREENSLADE BRITTON.

"An electrometric study of (*a*) the reduction of bromine with iodide ions, and (*b*) the oxidation of iodide ions with bromine, in aqueous solution." By H. T. S. BRITTON and H. GREENSLADE BRITTON.

"The potentiometric titration in acid solution of (*a*) potassium bromate with potassium bromide and (*b*) bromine in the presence of bromide ions with potassium iodide." By H. T. S. BRITTON and H. GREENSLADE BRITTON.

"A potentiometric study of the reaction between nitrous acid and hydriodic acid." By H. T. S. BRITTON and H. GREENSLADE BRITTON.

LOCAL REPRESENTATIVES OF THE CHEMICAL SOCIETY

Aberdeen.	J. M. C. Thompson, M.A., D.Phil., F.R.I.C., Chemistry Department, Marischal College, The University, Aberdeen.
Australia.	T. Iredale, D.Sc., F.R.I.C., The University, Sydney, Australia.
Birmingham.	L. L. Bircumshaw, M.A., D.Sc., Department of Chemistry, The University, Edgbaston, Birmingham, 15.
Bristol.	F. H. Pollard, B.Sc., Ph.D., A.R.I.C., Chemistry Department, The University, Woodland Road, Bristol.
Cambridge.	B. Lythgoe, Ph.D., Organic Chemistry Department, The University, Cambridge.
Canada.	W. D. McFarlane, M.A., Ph.D., The Laboratories, The Canadian Breweries Ltd., 496, Queen Street East, Toronto, 2, Canada.
Ceylon.	M. U. S. Sultanbawa, B.Sc., A.R.I.C., Department of Chemistry, The University, Colombo, Ceylon.
Edinburgh.	N. Campbell, D.Sc., Ph.D., Chemistry Department, King's Buildings, West Mains Road, Edinburgh.
Exeter.	S. J. Gregg, Ph.D., A.R.C.S., F.R.I.C., Department of Chemistry, Washington Singer Laboratories, Prince of Wales' Road, Exeter.
Glasgow.	J. C. Speakman, M.Sc., Ph.D., Chemistry Department, The University, Glasgow, W.2.
Hull.	Professor Brynmor Jones, Sc.D., Ph.D., F.R.I.C., University College, Hull.
India.	Sir Shanti S. Bhatnagar, O.B.E., D.Sc., F.R.S., Secretary, Ministry of Natural Resources and Scientific Research, New Delhi, India.
Irish Republic.	V. C. Barry, D.Sc., F.R.I.C., Medical Research Council of Ireland, The Laboratories, Trinity College, Dublin.
Leeds.	P. A. Briscoe, B.Sc., A.R.I.C., Organic Chemistry Department, The University, Leeds, 2.
Liverpool.	W. B. Whalley, B.Sc., Ph.D., F.R.I.C., Organic Chemistry Department, The University, Liverpool.
,,	L. A. Haddock, M.Sc., F.R.I.C., Imperial Chemical Industries, Ltd., Research Department, Widnes Laboratory, Widnes.
Manchester.	G. R. Barker, B.Sc., Ph.D., Chemistry Department, The University, Manchester, 13.
,,	M. A. T. Rogers, B.Sc., Ph.D., A.R.I.C., Imperial Chemical Industries, Ltd., Hexagon House, Blackley, Manchester.
Newcastle and Durham.	G. A. Swan, B.Sc., Ph.D., F.R.I.C., Department of Chemistry, King's College, Newcastle-on-Tyne, 1.
New Zealand.	Professor F. G. Soper, C.B.E., D.Sc., Ph.D., F.R.I.C., University of Otago, Dunedin, New Zealand.
Northern Ireland.	H. Graham, D.Sc., A.R.I.C., 26, Malone Hill Park, Belfast.
North Wales.	W. Rogie Angus, M.A., D.Sc., Ph.D., F.R.I.C., Department of Chemistry, University College of North Wales, Bangor.
Nottingham.	D. O. Jordan, M.Sc., Ph.D., A.R.I.C., The University, University Park, Nottingham.
Oxford.	H. M. N. H. Irving, M.A., D.Phil., F.R.I.C., Inorganic Chemistry Laboratory, South Parks Road, Oxford.
Pakistan.	M. I. D. Chughtai, M.Sc.Tech., Ph.D., A.R.I.C., Punjab University Institute of Chemistry, The Mall, Lahore, Pakistan.
St. Andrews and Dundee.	H. T. Openshaw, M.A., D.Phil., Chemistry Department, United College, St. Andrews.
Sheffield.	A. H. Lamberton, B.Sc., Ph.D., Chemistry Department, The University, Sheffield, 10.
South Africa.	Professor W. Pugh, Ph.D., B.Sc., F.R.I.C., Chemistry Department, University of Cape Town, Rondebosch, S. Africa.
Southampton.	K. R. Webb, B.Sc., Ph.D., A.R.I.C., University College, Southampton.
South Wales.	K. W. Sykes, M.A., B.Sc., D.Phil., Department of Chemistry, University College, Singleton Park, Swansea.

H. K. LEWIS & Co. Ltd. BOOKS ON THE CHEMICAL AND ALLIED SCIENCES

Scientific and Technical Books :: Large Stock of Recent Editions :: Catalogue on Request
Foreign Books not in stock obtained under Special Licence

LENDING LIBRARY Scientific and Technical

Annual Subscription from **Twenty-five Shillings** Prospectus post free on application

THE LIBRARY CATALOGUE revised to December, 1949, recently published. To subscribers 17s. 6d net., to non-subscribers, 35s. postage 1s. Bi-Monthly List of New Books and New Editions sent post free to subscribers regularly.

H. K. LEWIS & Co. Ltd., 136, Gower Street, London, W.C.1
Business hours: 9 a.m. to 5 p.m., Saturdays to 1 p.m.
Telephone: EUSton 4282 (7 lines)

SYMBOLS, SIGNS, AND ABBREVIATIONS

A Report by the Symbols Committee of the Royal Society (representing the Royal Society, the Chemical Society, the Faraday Society and the Physical Society) has been prepared to supersede the Report issued in 1937 by the Joint Committee of the Chemical Society, the Faraday Society and the Physical Society on " Symbols for Thermodynamical and Physico-Chemical Quantities and Conventions Relating to their Use ".

This Report, which was published in the Journal for June 1951, lists the Symbols, Signs, and Abbreviations recommended for British Scientific Publications.

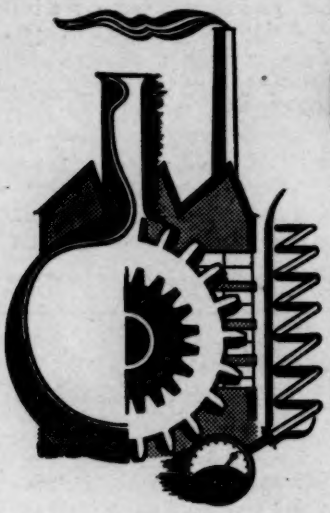
Reprints are available price 9d. per copy or 12s. per 25 copies (post free) from

The Chemical Society, Burlington House, London, W.1

MANSFIELD OIL-GAS PLANT
FOR LABORATORIES' GAS SUPPLY

Laboratories without a supply of gas should write for particulars of this Plant which produces gas in a simple manner from any cheap oil such as Solar Oil. . . . The gas produced has a calorific value of 1,350 B.T.U.'s per cubic foot, and is suitable for use with any appliance designed for use with coal gas and gives perfect oxidising and reducing flames.

MANSFIELD & SONS LTD
62 HAMILTON SQUARE, BIRKENHEAD



B.D.H.

Fine chemicals for industry

Hydrofluoric acid, all fluorides, lead dioxide, lead formate, sodium chromate—amino-guanidine sulphate, semicarbazide hydrochloride—cobalt salts, thallium salts, strontium salts—bromine compounds, alkyl halides, methyl mercaptan—are typical examples of B.D.H. Fine Chemicals for Industry.

B.D.H. Fine Chemicals for Industry are chemicals of laboratory purity for direct use as raw materials in industrial processes. We welcome enquiries for both organic and inorganic products required in high purity by the cwt. or by the ton.

THE BRITISH DRUG HOUSES LTD.

B.D.H. LABORATORY CHEMICALS GROUP

POOLE DORSET

Telephone: Poole 962 (6 lines) *Telegrams: Tetradome Poole*

LC/26

Journal of the Royal Institute of Chemistry & Journal of Chemical Society

PRINTED IN GREAT BRITAIN BY RICHARD CLAY AND COMPANY LTD. BUNGAY SUFFOLK.